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V-54
To June

JANUARY 1959

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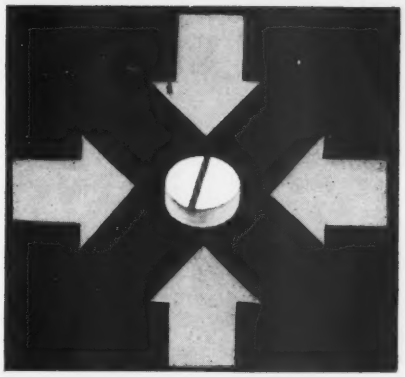

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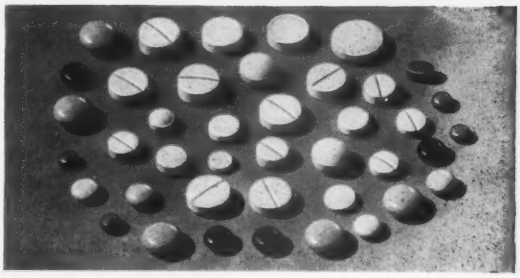

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Drug and Cosmetic Industry

Contents **January 1959 Vol. 84 No. 1**

Cover by Joel

Feature Articles

25 **Enzymes: Biochemical Jet Stream**
by Charles E. Dutchess, M.D.

28 **TGA Scientific Section Meeting 1958**

30 **Female Genito-Urinary Infections**
by Bernard Idson, Ph.D.

32 **Barrier Creams**
by Marvin K. Cook

34 **Anti-Inflammatory Steroids**

36 **Allantoin and Aluminum Derivatives in Dermatological Application**
by Irwin I. Lubowe, M.D., and S. B. Mecca

38 **Fragrant Aerosols—Ancient and Modern**
by E. R. van Liew and Victor Di Giacomo

40 **Measuring Skin Respiration**
by Henry Goldschmiedt, Ph.D.

Packaging and Selling Section

43 **The Professional Package Designer Comes of Age**
by Robert Sidney Dickens

45 **Aerosols Boost Over-all Sales**
by Arthur Kreinik

47 **Packaging and Selling**
by Frazer V. Sinclair

53 **Packaging News**

55 **Advertising Notes**
by Ted Klein

Departments

17 **Keeping Posted**
by Thomas R. Farrell

58 **Patent Thoughts and Trends**
by Thomas Cifelli, Jr.

63 **News**

74 **Management Forum**
by Francis Chilson

96 **Trade Literature**

104 **Industry's Books**
by Harry G. Kelbly

Technical Abstracts

by Joseph Kalish, Ph.D.

85 **Advancing Therapy**

90 **Perfumer's Shelf**

93 **Compounder's Corner**

98 **Skin Research**

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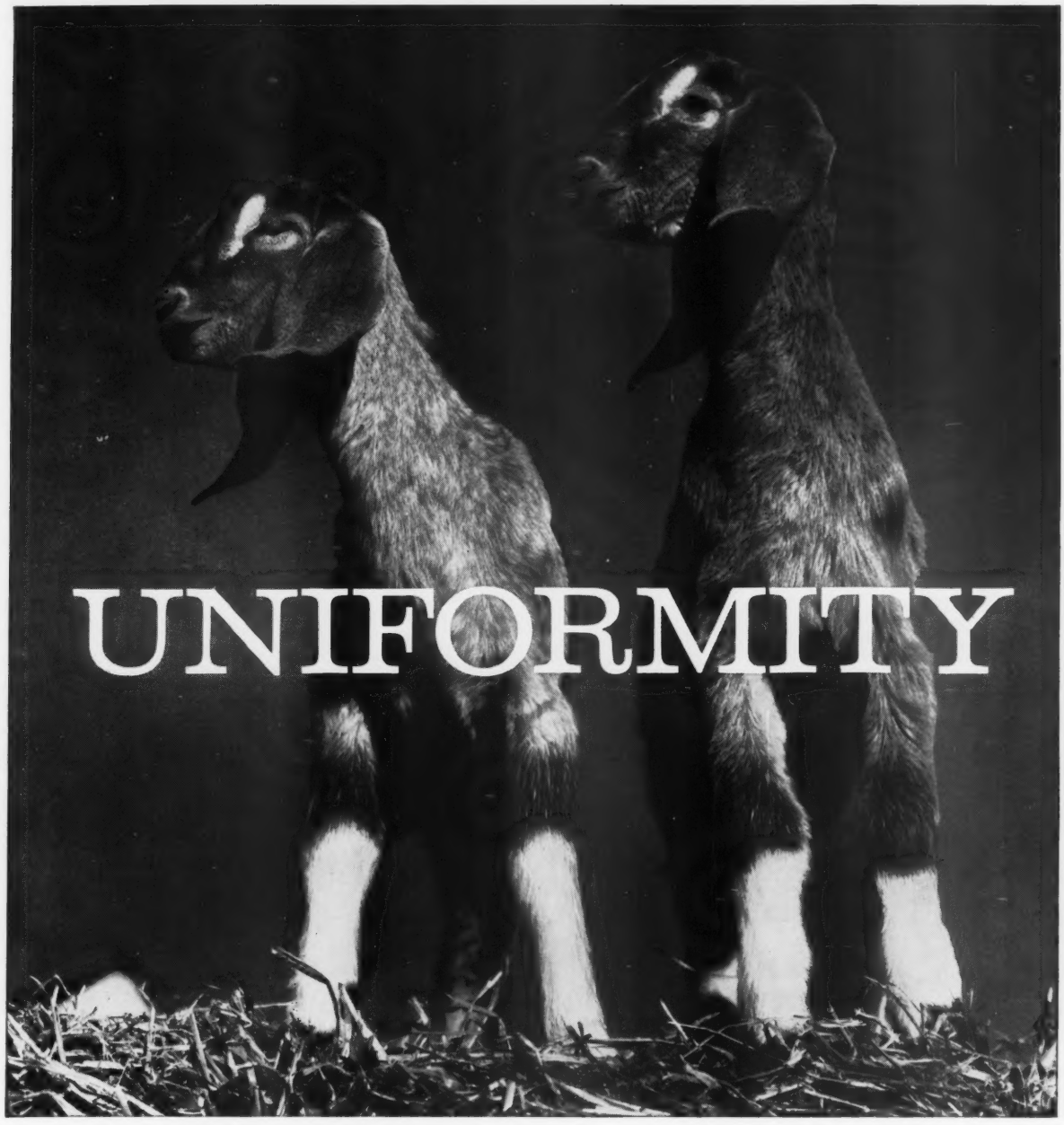

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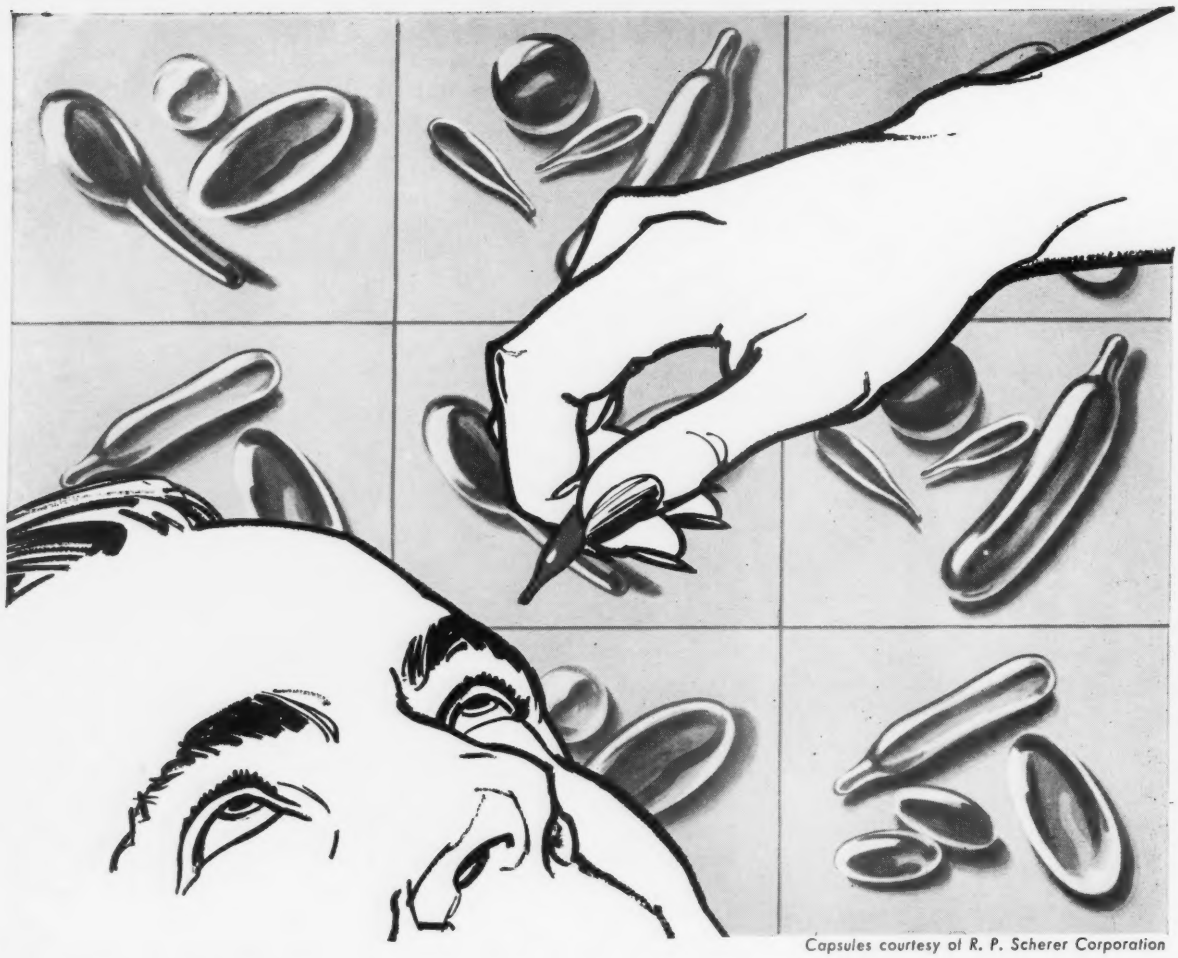

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Concentrated Imitation Butterscotch Flavor	2 ozs.
Concentrated Imitation Caramel Flavor	1 oz.
Imitation Tame Cherry Flavor 2:1	2 ozs.
Syntharome Imit. Wild Cherry Flavor Special	1/4 to 1/2 oz.
Imitation Wild Cherry Flavor 2:1	2 ozs.
Imitation Chocolate Aroma Flavor	2 ozs.
Cola Type Flavor 1:1	1/2 to 1 oz.
Cola Type Flavor 4:1	4 ozs.
Concentrated Lemon-Lime Flavor	1/4 to 1/2 oz.
Licorice Type Flavor 1:1	1/2 to 1 oz.
Syntharome Imitation Maplenut Flavor	1/2 oz.
Syntharome Imitation Raspberry Flavor	1/4 to 1/2 oz.
Syntharome Imit. Tutti-Frutti Flavor	1/4 to 1/2 oz.
Imitation Tutti-Frutti Flavor 2:1	2 ozs.
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Cherry Imitation	2 to 4 oz.
Cola Type	2 to 4 oz.
Grape Imitation	2 to 4 oz.
Lemon	2 to 4 oz.
Lemon-Lime	2 to 4 oz.
Lime	2 to 4 oz.
Loganberry Imitation	2 to 4 oz.
Maple Imitation	2 to 4 oz.
Orange	2 to 4 oz.
Pineapple Imitation	2 to 4 oz.
Raspberry Imitation	2 to 4 oz.
Root Beer	2 to 4 oz.
Strawberry Imitation	2 to 4 oz.
Tutti-Frutti Imitation	2 to 4 oz.

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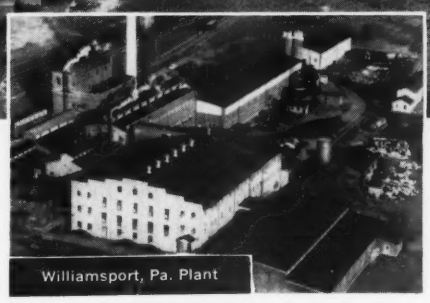

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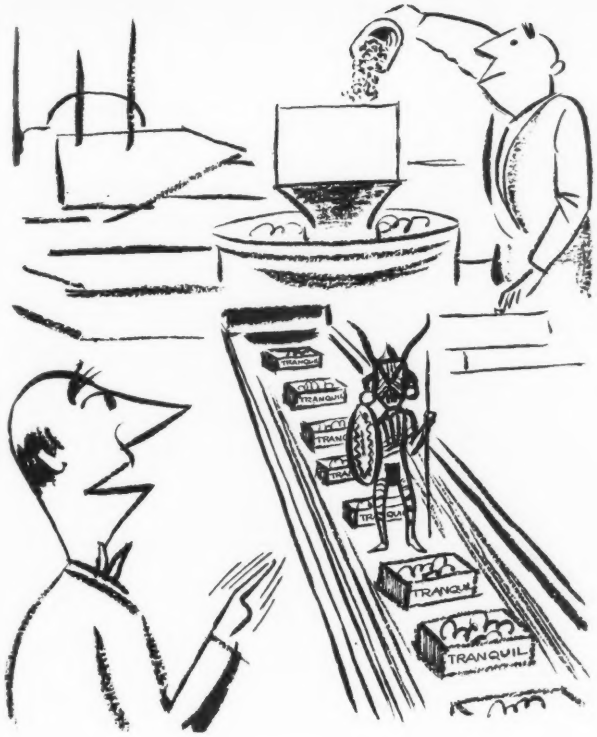

Keeping Posted

Pharmaceuticals for 1959

Standard and Poor's Corporation has issued its most recent analysis of the drug industry and concludes that the outlook remains bright. For 1959, the growth in industry sales can be expected to be about eight to ten per cent. This gain will arise from normal factors such as population increase, especially in the geriatric group; new products and improved forms of old ones; expanded use of drugs for human and animal use; further growth of foreign business.

The broad spectrum antibiotic market should advance about five per cent in the coming year over the previous $270 million. Tetracyclines account for more than half of the broad spectrum antibiotic sales. Vitamin unit sales should increase in geriatric use and in greater animal and human nutritional use, but foreign competition is expected to weaken prices and maintain sales value at $250 million. Tranquilizer sales are now estimated at $175 million, with government purchases for Federal and state institutions accounting for about 20 per cent of the total. Rauwolfia products are expected to decline slightly, mild tranquilizers like meprobamate seem to be holding their own, while the phenothiazine derivatives are increasing their sales. The $95 million corticosteroid market should benefit from the introduction of dexamethasone.

Merck's Diuril diuretic is now estimated to be selling at an annual rate of $25 million and increasing, and Upjohn's Orinase oral antidiabetic has an estimated volume of $15 million. The total antidiabetic market, including $20 million of insulin, may be about $50 million.

Product Liability and Implied Warranty

Everett I. Willis of the law firm of Dewey, Ballantine, Bushby, Palmer and Wood discussed product liability and the legal doctrine of implied warranty at a meeting of the National Drug Trade Conference. Product liability risks are becoming greater, not only because of court interpretation of the law, but also because new drug products are being marketed with increasing speed by the drug industry. Our social philosophy now is permitting consumers to recover from producers. The speaker said, "It seems to me that these problems are more likely to increase than to diminish over the next few years. The day may come when manufacturers and sellers of newly-discovered drug products find themselves facing an almost unlimited risk of liability, a risk which cannot be avoided even by the most meticulous care, which cannot be adequate insured against and which cannot be effectively disclaimed."

Chanel Counterfeiter Caught

New York police picked up a counterfeiter who had been selling labelled bottles imitating Chanel No. 5 perfume. The counterfeiter admitted, according to a story in the "Daily News," to sales amounting to $4,320 at the rate of $2 an ounce. His base of operations was a Brooklyn apartment in which the "perfume" was manufactured in the bathtub; sales outlets were New York poolrooms.

Cheminform Institute

The Cheminform Institute, Coliseum Towers, New York City, has been organized by H. Bennett and E. Rosendahl, formerly of Glyco Products. It maintains a file of trademarks in the chemical and allied fields, including registered, unregistered, common, trivial, foreign and scientific names in every type of chemical and chemical-using industry. The service is international in scope.

Coordinated Drug Promotion

Reminiscent of the great Terramycin operation, Pfizer is moving fast with its new oral antidiabetic drug,

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. . . formulate your toiletries with ***Dow Corning Fluids***

Here's what your cosmetic products can gain from silicones . . . greater and longer-lasting effectiveness in use; protection against water-borne irritants; more pleasing application characteristics. In lotions, Dow Corning silicone fluids also improve and speed spreading, and virtually eliminate stickiness and oiliness. Countless cosmetics, from hair sprays to hand creams to pre-shave lotions, have already gained a sales edge by using — and marketing the name of — silicones. How about your products?

Dow Corning silicone fluids are specifically developed for cosmetics; they are odorless, physiologically harmless, inert, and non-rancidifying. For further details, samples and data, contact our nearest branch office or write direct.

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Diabinese. "The Journal of the American Medical Association" carried a 24 page insert, the largest continuous-page advertisement ever carried by the Journal, as a technical bulletin reproducing exhaustive clinical information provided at a recent symposium. The availability of Diabinese had been previously announced in other ethical medical journals and detail men reviewed the report with physicians. Long before the product became available, mailings informed retail, wholesale, government and hospital pharmacy personnel of the drug's properties and uses. Representative calls and advertisements in pharmacy journals, reinforced the message.

Matchabelli Plant to Close

Chesebrough-Pond's Inc., announced that it will terminate operations at its Prince Matchabelli Inc., plant in Bloomfield, N. J. during the summer of 1959.

The acquisition gave Chesebrough-Pond's duplicate facilities and overhead expenses at Bloomfield. The manufacturing and distribution of the Seaforth and Matchabelli product lines will be continued at Clinton, Conn. Engineering and cost analysis studies indicated that operation of the Bloomfield plant is neither practical nor economical on a continuing basis.

The parent company will make a separation allowance based on years of service with Prince Matchabelli, will pay accrued vacation pay, and will make provisions for conversion of group life insurance and hospital-surgical insurance coverages. In addition, the company will work with various state and regional Government agencies and with local industry, to try to place employees in new positions, and secure immediate attention to the processing of unemployment compensation applications.

Colgate Acquires Wildroot

Colgate-Palmolive Company and Wildroot Company, Inc. have agreed to the acquisition of Wildroot by Colgate. All outstanding shares of Wildroot will be exchanged for Colgate stock, a transaction probably involving in excess of $10,000,000, and operations are expected to continue in Buffalo.

Warner-Lambert and Reynolds Merger Cancelled

The proposed merger between Warner-Lambert Pharmaceutical Company and R. J. Reynolds Tobacco, which had apparently progressed to the point where only relatively minor details were still under discussion, has been cancelled. The joint statement by Elmer H. Bobst and Alfred E. Driscoll of Warner-Lambert and John C. Whitaker of Reynolds stated: "Some time ago R. J. Reynolds Tobacco Company approached Warner-Lambert Pharmaceutical Company suggesting discussions leading to a possible merger of the two firms.

"Following several months of study, the management of both companies, although having developed a high regard for each other, concluded, since it did not seem possible to reach agreement on certain aspects of the proposed transaction, not to proceed further with discussions. Accordingly they have been amicably terminated."

Did the respective managements ask themselves the same questions about the feasibility of the plan that the trade had been asking and finally decide that diversification has its limits? An anomaly worthy of note is that the prices of Warner-Lambert common stock went up fast on rumor and then confirmation of the merger plan, but dropped only temporarily and then climbed again when the news of the cancellation came out.

Schering Acquires Veterinary Company

The Schering Corporation's acquisition of American Scientific Laboratories, Inc., Madison, Wisconsin, was made effective with the issuance of Schering common stock in exchange for all of the outstanding stock of American Scientific Laboratories.

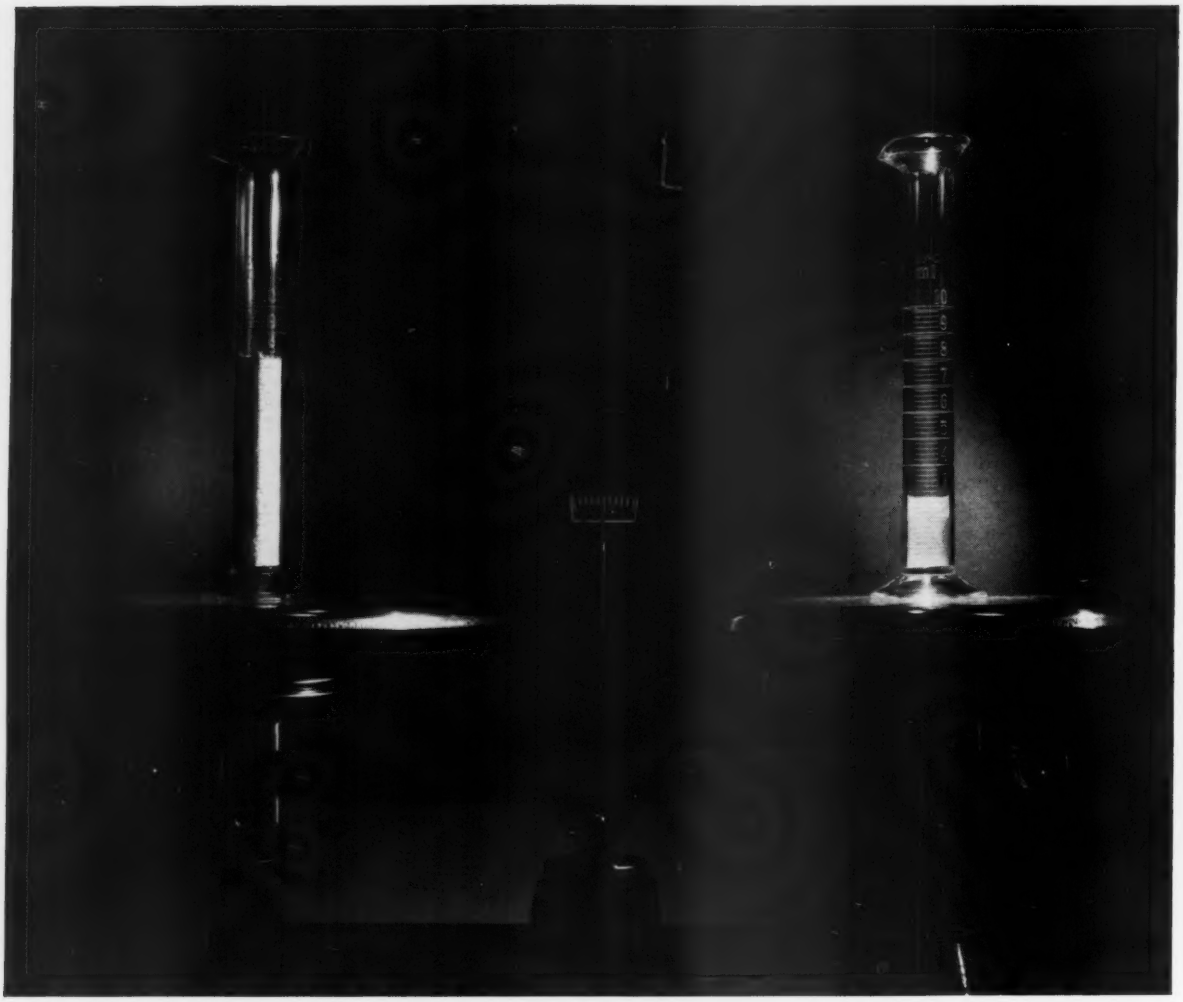
The Wisconsin company produces veterinary biologicals, pharmaceuticals and pesticides with sales currently at an annual rate of approximately $1½ million. It will be operated as a wholly-owned subsidiary of Schering, continuing at the present location and under its present management.

Aspirin Statistics

According to the U. S. Department of Commerce, production of acetylsalicylic acid in 1958 reached an all-time high of 20 million pounds. At the rate of 7,000 grains to the pound, five grains to the tablet, this could be translated into about 28 billion aspirin tablets or 14 billion aches. From the present state of the world, we would guess this to be a conservative estimate. For additional arithmetic doodling, a standard aspirin tablet would be seven-sixteenths of an inch in diameter and one-sixth of an inch thick. End-to-end, then, our billions of aspirin tablets would circle the world just about eight times. One on top of the other they would make a very unstable column reaching more than one-fourth the distance to the moon.

The Proprietary Association Meetings

The Proprietary Association held its annual Research and Scientific Development Conference and its Fifth Small-Volume Forum in New York City in December. Association president Robert B. Brown of Bristol-Myers opened the conference, which was held at the Sheraton-McAlpin Hotel and Robert G. Sanders of the Warner-Lambert Pharmaceutical Company presided as chairman of the Scientific Development Committee. The conference had the largest attendance on record. Six papers were presented. In the morning session, talks were given by Paul K. Smith on over-the-counter labeling; by Ernest Allen on



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government-supported research and on laxatives by Almy and Sleisinger. In the afternoon, George Wolcott spoke on clinical research and Grafton D. Chase presented a paper on radioisotopes in pharmaceutical research.

Medical Care Expenditures

Data available from the U. S. Department of Commerce and the Health Information Foundation show that aggregate personal expenditures for medical care increased from almost $3 billions in 1929 to $15 billions for 1957 despite a drop below $2 billions for 1933. Average disposable personal income per capita was $683 in 1929, $1,812 in 1957, while corresponding medical care expenses were $24 and $89, respectively. Included in the total, expenditures for physicians' services were $959 millions or $7.89 per capita in 1929, $3,693 millions or $21.93 per capita in 1957, while dental expenditures were $482 millions ($3.97 per capita) in 1929 and $1,705 millions ($10.09 per capita) in 1957. Hospital expenses amounted to $403 millions in 1929, at the rate of $3.31 per capita and $3,884 or $23.07 per capita in 1957. The cost of hospitalization insurance was $108 millions in 1929 and $1,064 millions in 1957. Expenditures for drug preparations and sundries were $604 millions in 1929, $3,098 millions in 1957, or per capita rates of $5.00 in 1929 and $18.33 in 1957.

From 1929 to 1957, disposable income increased by a factor of 2.65; per capita total expenditures for medical care increased 3.71 times. Of these total costs, physician expense was 2.78 times greater; dentist expense was 2.54 times greater; expenditures for drugs were 3.67 times as great, while hospital costs were 6.97 times as great.

Plough Makes Grant for Leukemia

Plough, Inc., Memphis drug manufacturer, has made the first research grant to St. Jude Hospital to begin immediate study into the causes of leukemia and other childhood diseases.

The company made a grant of $10,000 for research in the field of pediatric hematology and allied blood diseases, even though construction has not yet begun on the two-million dollar St. Jude Hospital.

SKF Sets Up Foreign Research

Smith Kline & French Research Institute of Great Britain has been set up as an independent research group, to supplement the company's Philadelphia operation and for greater proximity to European research. The new organization will be housed in a $2 million building now under construction and will eventually have a staff of 40. It will report directly to the parent company's research vice-president, but will have virtual autonomy in carrying out its own program.

The originally lower cost expected for overseas research will turn out to be less of an advantage than hoped, since overhead costs are not substantially lower. The advantage of location may well strengthen the SKF position with respect to new products, since Thorazine was first synthesized by Rhone-Poulenc in France, Cytomel was pioneered in England and Darbid grew out of Dutch research.

Cancer Chemotherapy

The "massive effort" to discover chemical compounds that will be effective and safe in the treatment of cancer is now in full scale operation, according to HEW Secretary Flemming. Hospitals, universities, research laboratories, industry and government are cooperating in the program which is being directed by the Public Health Service through its Cancer Chemotherapy National Service Center. The program has been steadily expanded over the past 5 years.

Over 40,000 compounds and other materials are being tested annually on more than a million mice to uncover chemicals with anti-cancer properties. So far some 70,000 materials have been put through screening tests. Between 400 and 600 materials a year are showing enough promise to be given further analysis, with tests on larger animals. Nine out of 10 materials are rejected in this process either as ineffective or too toxic for human use. About 40 materials a year are approved for clinical trials with human patients in about 150 cooperating hospitals in the U. S. Currently about 70 materials are undergoing clinical trials.

So far none of the drugs being tested has proved to be a cure for cancer.

FTC Penalties

The Federal Trade Commission announced that civil penalty suits involving violations of FTC orders to cease and desist have resulted in financial penalties. In the most recent case, the U. S. Court of Appeals for the Fifth Circuit affirmed a judgment of $8,000 against Sidney J. Mueller, trading as Mueller Hair Experts, Houston, Texas, for violation of an order against the false advertising of hair and scalp treatments and preparations used for such purposes. The U. S. District Court for the Southern District of California entered a judgment of $1,500 against Paul R. Dooley, Inc. and Dooley Hair Experts, Inc., San Diego, Calif., for violating an order prohibiting them from misrepresenting the benefits provided by their hair and scalp preparations.

Refusing Advertising

The right of media to refuse advertising has had additional confirmation from a recent New York Supreme Court decision, as reported and discussed in "Media/scope." In this instance, a newspaper refused an advertisement that mentioned prices below the fair trade level, even though the advertiser had a

When Vitamins get together...

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But... NYQ DRY VITAMINS

behave like little angels!

Write today for samples of these NYQ DRY VITAMINS!

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DRY VITAMIN D_2
DRY VITAMIN A and D_2
DRY CYANOCOBALAMIN
DRY COBALAMIN CONCENTRATE
DRY VITAMIN E ACETATE 25%
DRY VITAMIN E ACETATE 33%
(Granular and Fine Powder)

NYQ *gelatin*-encapsulated vitamins minimize potency-robbing interreactions among vitamins and other ingredients in your preparations.

You get uniform dispersion so that every tablet contains the proper amount of each vitamin. Loss on extrusion is low, potency is protected and stability is assured for longer shelf-life.

Need for costly overages is greatly reduced.

Very important: the *gelatin* matrix in NYQ dry vitamins doesn't interfere with physiological availability! It's ideal for soluble tablets, too, and won't cause unpleasant after-taste. IDEAL FOR BABY FORMULAE.

We will gladly submit generous samples and suggest formulation techniques. Deliveries are always made immediately from five coast-to-coast stockpoints.

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contract with the publication. The publication had the right, however, to approve subject matter, form, size, wording, illustration and typography of all advertising so that the judge concluded that the publication had the broadest discretion to reject copy without limitation. The Court concluded that the publication had a reasonable right to refuse advertising that might have involved the publication in litigation. This is in contrast to a 1951 court decision in which the publication was not permitted to refuse advertising since the reason for refusal was an illegal one based upon the publication's "bold, relentless, and predatory commerical behavior." The matter currently seems to boil down to permitting media to refuse to accept advertising on the basis of any reasonable policy not aimed at an illegal result.

FTC Antibiotics Hearings

Hearings have begun in New York on the formal complaint by the Federal Trade Commission of monopolistic practices, price-fixing and restraint of trade in the sale of antibiotics. Under the hearing examiner, Robert L. Piper, exhibits have begun to be submitted, with witnesses to be called later. Early sessions were devoted to determining the nature of the data to be submitted under subpoena, the companies holding out against what they considered to be non-pertinent material that might reveal competitive trade secrets. The hearings must inevitably be protracted, with the final decision a long way off. Attorneys for the Government are Andrew C. Goodhope, Lars E. Janson, E. G. Barnes, Daniel Hanscom, Arthur Edgeworth and J. J. Gercke. American Cyanamid Company is represented by Ralstone I. Irvine, Richard Y. Holcomb, Samuel W. Murphy, Jr. and Walter R. Mansfield of Donovan, Leisure, Newton and Irvine. Counsel for Bristol-Myers Company and Bristol Laboratories, Inc. include Allen T. Klots, Peter H. Kaminer and Merrell E. Clark, Jr. of Winthrop, Stimson, Putnam and Roberts with Henry J. Zafian while Chas. Pfizer & Co., Inc. is represented by John Wood and Charles E. Stewart, Jr. of Dewey, Ballantine, Bushby, Palmer and Wood along with Arthur G. Connolly. Attorneys for Olin Mathieson Chemical Corporation were Allen F. Maulsby and Alan J. Hruska of Cravath, Swaine and Moore while the Upjohn Company was represented by Gerhard A. Gesell and William F. Baxter.

Mailings to Physicians

A mail survey was conducted by Medical Advertising Service of New York to learn more about the doctor's routine and attitude on the direct mail he receives. A total of 3241 cards were sent to general practitioners, and every state was covered. Replies to almost 49 per cent of the cards demonstrated that physicians do read their direct mail.

Of the 1508 physicians who responded, 759, or a little better than 50 per cent, stated that they opened their own mail; of the 749 secretaries or nurses who opened the mail, about half passed all the mail to the doctors while 470 selected mail to be passed on. Thus, 74 per cent of those responding this survey at least saw all of their mail. Concerning the value of the mail, almost two-thirds felt that 40 per cent or less of the mail received was of value and more than 200 made critical comments.

McKeen Awarded Italian Doctorate

John E. McKeen, president of Chas. Pfizer & Co., Inc., has been awarded an honorary doctorate in Agricultural Sciences by the Catholic University of the Sacred Heart in Milan, Italy. The degree, first such honor to be awarded to an American by the university, was conferred on Mr. McKeen in recognition of his contributions to the "chemical and biological sciences" through studies conducted by Pfizer in the agricultural field.

Drug Industry Attacks

A public relations spokesman for the drug industry recently expressed grave concern over attacks on drug industry prices and practices and he thought that these hinted at a widespread drive to put over a form of socialized medicine. Printed attacks were described as a form of left-wing journalism which permits detractors to use the part of the story that is derogatory and omit the favorable slants. A number of recent fiction attempts have given luridly colored versions of the industry. Most of all, the blame is laid at the door of "congressional publicity hunters" seeking to cause trouble in matters of pricing and collusion. The suggestion was made that the industry should refuse to allow itself to be sidetracked into being concerned with smaller attacks but should pick holes in and respond to major assaults.

Congressional spokesmen, on the other hand, disavow responsibility for originating attacks on high pharmaceutical prices. They maintain that investigations are a response to public outcry.

Actually, the pharmaceutical industry, like the medical profession, might profit from an objective look at itself. The great public health contributions made by the industry are certainly true and so are the large and speculative spendings for research. But just as true is the fact that the industry exists to make a profit and this aspect certainly need not be kept under cover. In the United States we most certainly believe in the profit system. High prices are not directly caused by high research costs, as is so often implied. The relationship is much more indirect. We must convince people that their lives are being prolonged by the results of expensive and often futile research which is paid for only by attracting capital that requires more than ordinary rates of return. The drug industry, in its present scientific form, is young, vigorous, alert and willing to gamble its time and money, but is not willing to gamble with the health

and well-being of the public. The industry needs and is entitled to its profit margin to permit it to manufacture and distribute products with the extreme speed the doctors and patients demand. Marginal prices (as in penicillin) and little or no profits will quickly squeeze originality and enterprise in research, production and merchandising, out of the industry. On the other hand, there is no need for the industry stubbornly to present its worst face. The patient may remember only that the prescription cost him $20, not that he was saved a $1,000 hospital bill. He might be less unhappy if he could buy two prescriptions, at different times, for $10 a piece. A more difficult industry problem is its close relationship with physicians and pharmacists, in which the industry may be blamed for situations outside of its control. Improvements come, however, not from easy words but from honest self-appraisals.

Secretary Flemming Holds FDA Conference

Representatives of trade associations in the drug industry met with HEW Secretary Flemming at an all-day, informal conference in December to discuss matters which they felt should be brought to the attention of the Secretary relating to the Food and Drug Administration and its enforcement activities. Several speakers praised the work of the Food and Drug Administration and urged that the FDA budget be increased so that a more efficient job can be accomplished.

A few speakers directed their thoughts to the desirability of obtaining a successor to Albert H. Holland, the Medical Director of the Food and Drug Administration, who would be qualified not only as an administrator but who would be thoroughly oriented in problems of research. Reference was made to the career service people in the FDA and at least one speaker urged that political considerations should not enter into the choice of the Medical Director of the FDA. On this point Commissioner Larrick stated that he was particularly well satisfied with the present situation in HEW and referred to the fact that Secretary Flemming had for nine years been a member of the Civil Service Commission.

Representatives of retail pharmacy devoted some attention to the question of the transfer of prescription legend drugs to over-the-counter. It was urged that careful consideration be given to the public health problems involved in relation to over-the-counter labeling. At least one spokesman for retail pharmacy strongly emphasized that their interest was not "economic" but was based upon the public health aspects of permitting products to be sold to laymen rather than through the Rx legend route.

It was recommended that if there is to be new-device and new-cosmetic legislation in the future—and these two matters are obviously on the legislative calendar of FDA—that it be done slowly. It was pointed out that the FDA has a man-sized job on its hands now to administer the new Food Additives Amendment and all its ramifications, and that it should take time to get it to be a "perfect Act," that these matters should be thoroughly clarified before proceeding with others. The Commissioner did not necessarily assent to this suggestion but there was an inference that this recommendation would be thoroughly considered.

Representatives of the consumer interests spoke of the desirability of the FDA considering the efficacy of a new drug at the same time that a New-Drug Application is screened for safety. FDA officials present spoke of the screening of new drugs for efficacy, but pointed out that the safety angle was the basic requirement of the New-Drug Application procedure. At the consumers session with the Secretary the next day, it is understood that considerable attention was given to the question of advertising of o-t-c and Rx legend products, and it is also understood that recommendations were made to place the control of the advertising of drugs under the Food and Drug Administration rather than the Federal Trade Commission.

Vitamin Supplements

A news release put out by the American Medical Association made the headline assertion "vitamin supplements unnecessary for most persons." Dr. Robert S. Goodhart, scientific director of the National Vitamin Foundation, comments on this. He asserts that nowhere in the release or in the statement of the Council on Foods and Nutrition of the American Medical Association is the statement made in those words. The assertion in fact is that vitamin supplementation is unnecessary for normal persons following an adequate diet, fulfilling the Recommended Dietary Allowances of the National Research Council. The Foundation does not deny that most "normal" individuals can maintain health with a diet meeting these Recommended Dietary Allowances; it asserts, however, that many people do not get such a diet. The Vitamin Foundation believes "As preventive medicine, as a public health measure, the average person should take vitamin supplements simply because neither he nor his physician has any readily available way of determining his requirements, and he has no way of knowing how good his diet is."

Mailing Drugs

The Food and Drug Administration re-emphasizes that drug producers are legally responsible for making sure that they ship prescription drugs only to persons authorized to distribute and dispense them. A Philadelphia company has been convicted of shipping drugs in interstate commerce to a Virginia chiropractor not licensed by his state to dispense drugs; the FDA at the same time learned that the company was selling dangerous prescription drugs to another unauthorized individual, who was convicted and fined, as also were two others, who had purchased drugs from him for resale.

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One of America's leading producers of pharmaceutical chemicals, Heyden Newport can assure you of the quality and quantity – in the form and grade to meet your particular requirements.

Heyden Newport chemicals are found in a long line of familiar products – serving as analgesics and antipyretics; counter-irritants in liniments and ointments; preservatives; flavoring agents in toothpastes, confectionaries and tobaccos; perfume ingredients and intermediates; and sun-screening agents for suntan lotions and creams – to name a few.

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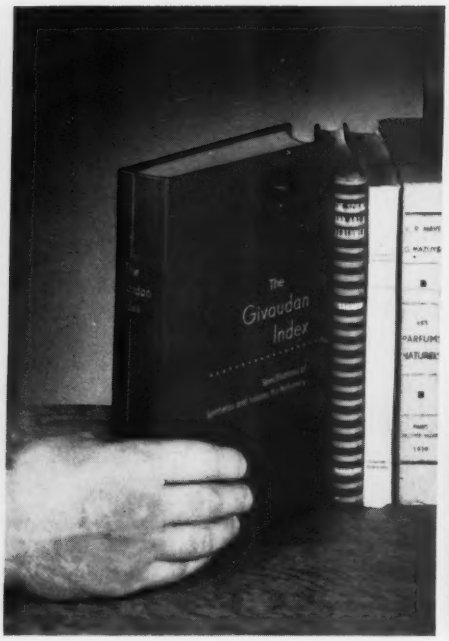
New Givaudan odors created by synthesis are steadily broadening the scope of the perfumer's skills. Examples are the Givaudan musks, unsurpassed for quality and variety.



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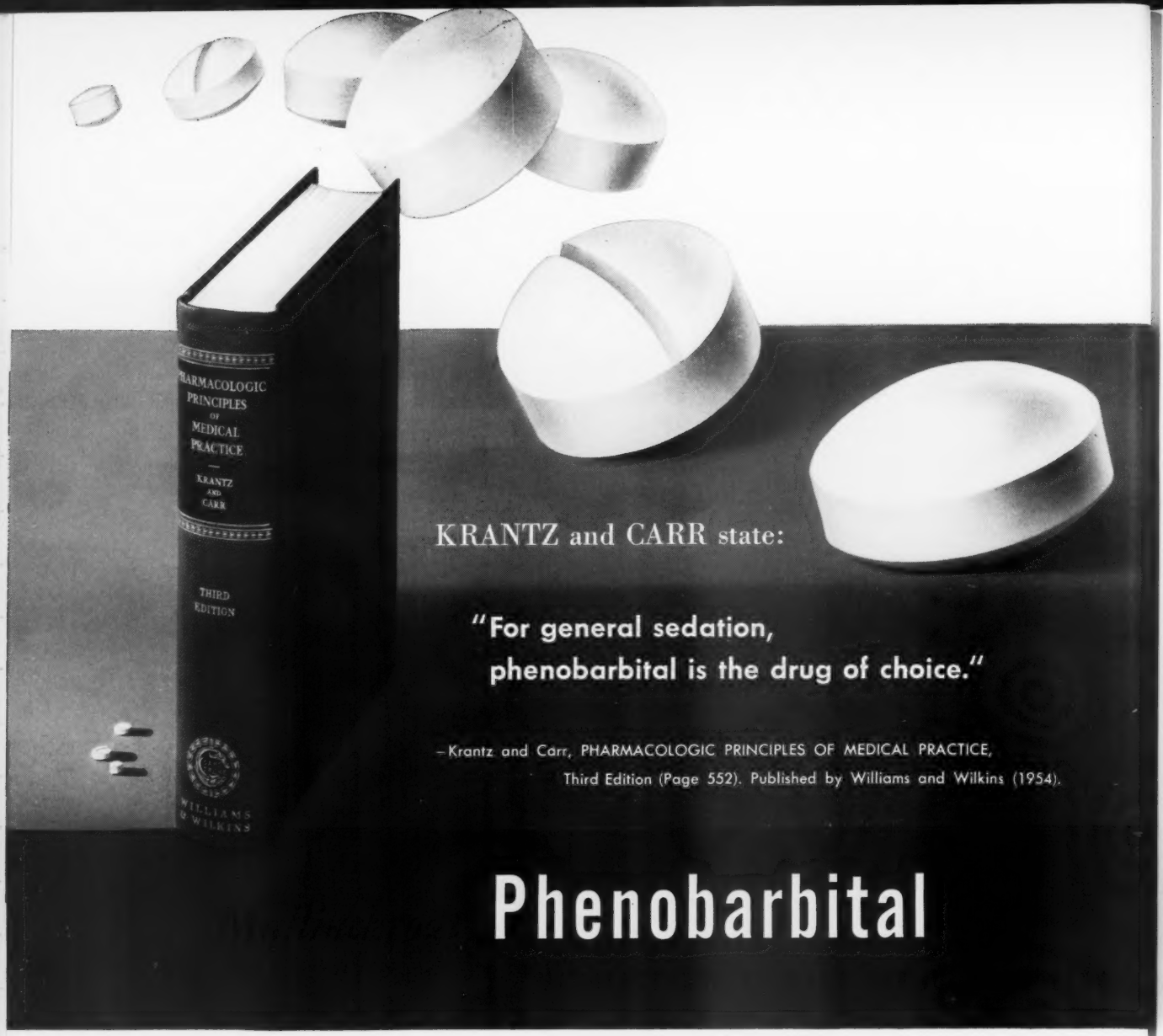

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If the present era of biochemistry needs a general characterization, it might be said that the central problems are those concerned with enzyme action.

CARL F. CORI

Life, to the enzymologist, may appear to result from the integrated activity of a host of enzymes, and the cell to be the smallest and simplest unit in which complete integration is accomplished. . . . What makes a cell complex, then, is the multitude of its parts—in this case of its enzymes—and the limited space in which they must operate.

GEORGE E. PALADE

In turn the enzymes have proved to be tools of such breath-taking elegance and simplicity as to revolutionize the tactics of determining structure or of analyzing for minute amounts of material. . . . The concept of the mitochondrion as an organized mosaic of several hundreds of enzymes linked together structurally as well as functionally and with unique operational principles is now well established in biochemical thinking. . . . A fabulous area of exploitation awaits the investigators who can hurdle the conceptual barriers in the way of the biochemical study of hormone action at the molecular level.

DAVID E. GREEN

The problem of enzymes encompasses essentially the whole of biology. When we understand enzymes —their structure, the mechanism of their synthesis, the mechanism of their action—we shall understand life.

LINUS PAULING

ENZYMES
Biochemical Jet Stream

BY CHARLES E. DUTCHESS, M.D., INDUSTRY CONSULTANT, CONSULTANT TO WALLERSTEIN LABORATORIES, INC.

About the most exciting thing in the pharmaceutical industry nowadays is not the new tranquilizers, or the "oral insulins," or the new steroids, or the new antimicrobials, or the new hypotensives and diuretics. It's really not any one new product or group. It's the new—to most of us—science that has been mushrooming like an atomic cloud, enzymology. And as the spectators of the first atomic explosion found it difficult to grasp its significance and express their feelings, the reader who first looks into enzymology is overwhelmed by its magnitude and complexity, and finds it hard to find any way of beginning a communication concerning this stupendous swarm of biologic activities.

As a practical application of available facts there is nothing new about enzymology. The action of yeast in "raising" dough was familiar enough to lead Paul, the Biblical author, to cite it in both Corinthians and Galatians as a truism, "A little leaven leaveneth the whole lump." And long before that the leavening of bread was standard practice. For thousands of years man has made use of enzyme-producing microorganisms in baking and in the mysterious processes that make wines and cheeses.

In modern times industry has long been utilizing enzymes in numberless practical ways. As the well-known science writer J. D. Ratcliff[1] put it, "They (enzymes) have been put to work providing stronger cloth, better leather, clearer beer and clearer wine, lighter bread, and a brilliant array of life-saving drugs. . . ."

ALL PHOTOS COURTESY WALLERSTEIN LABORATORIES, INC.

Carlyle Gantz, laboratory expert, inspecting a multiple-unit mash bath used in analysis and evaluation of malt and cereal adjunct samples.

Enzymes are used as meat tenderizers, as solvents, even as spot removers. They are invaluable in baking, in brewing, in leather tanning, in production of citric acid, steroids, alcohol, acetone, lactic acid and many other chemicals. And even the great industrial use now made of these willing workers is probably small compared to their coming use in future years.

In pharmacy and medicine the useful activity of enzymes has led to the development of a surprising number of trade-marked products. Since digestive enzymes were discovered long ago, and since diges-

After mashing, the worts obtained from malt or cereal adjunct samples are filtered for observations of clarity, color and extract. Here the equipment is being checked by Charles Hahn, supervisor of the laboratory.

tive complaints have always been prevalent, digestive enzymes were utilized early and have continued to form the basis of most of the enzyme products marketed today. These include pepsin, pancreatin—

EXAMPLES OF TRADE MARKED ENZYME PRODUCTS

Miscellaneous

- Alidase (Searle)
- Enzeon (Breon)
- Hyazyme (Abbott)
- Neutrapen (Schenley)
- Panafil (Rystan)
- Parenzyme (National Drug)
- Tryptar (Armour)
- Wydase (Wyeth)

Digestive

- Varidase (Lederle)
- Analeptone (Reed & Carnrick)
- Chymar (Armour)
- Caripeptic Liquid (Upjohn)
- Carizyme (Buffington's)
- Convertin (Ascher)
- Doxygest (Breon)
- Entozyme (Robins)
- Enzypan (Norgine)
- Geriatrone (U. S. Vitamin Corp.)
- Pepsolac (Pitman-Moore)
- Peptenzyme (Reed & Carnrick)
- Plurizyme (Nelson-Boyer)
- Taka-Diastase (Parke, Davis)
- Trypsogen Enterosol (Carnrick)
- Zyme-Essen (Brewer)

which supplies amylolytic, proteolytic, and lipolytic enzymes—and such other things as diastase made by the fungus *Aspergillus oryzae*, and papain, which is derived from the juice of a tropical plant.

The protein-digesting action of certain enzymes such as papain has been utilized in products applied to aid in cleaning up burns, bed sores and chronic ulcers, and thus to expedite their healing. Examples of such products are Chymar (Armour), Panafil (Rystan), and Varidase (Lederle).

We find a newer and more spectacular application of enzymology in the type of treatment now being given to dissolve intravascular blood clots. This is expected to be life-saving in many cases of cerebral and coronary thrombosis. Such studies are being made with Lederle's buccal tablets of streptokinase, and National Drug's buccal Parenzyme. Being proteins, enzymes are large molecules, and it seems as yet inexplicable that such substances can apparently penetrate the oral mucosa and thus be picked up by the capillary circulation for action at some distant point in the vascular tree.

Dr. Paul Ruegsegger of the Sloan-Kettering Institute, New York City, has reported that plasmin, a substance extracted from human blood, has been shown to have the ability to dissolve clots, and to be safe for use. Sherry has recently reported using streptokinase in 80 patients. This substance, produced by Lederle, appears to "activate" the blood to produce plasmin. Plasmin is being made in experimental quantities by Merck Sharp & Dohme; Ortho; and Parke, Davis & Co.

One of the abnormalities, namely, mental retardation, attributed to an inborn error of enzyme metabolism has not yet been named. In the urines of a four-year-old girl and her seven-year-old brother re-

ported by Allen, Westall isolated large amounts of arginino-succinic acid. According to Westall, the large amounts of this metabolite appeared because the enzyme that normally monitors its conversion to urea was congenitally absent.

A particularly interesting facet of enzymology is connected with human diseases that may be caused or influenced by enzyme actions or deficiencies. For example, at a recent meeting of the American Heart Association, Milton Mendlowitz suggested that lack of a specific enzyme may be the actual cause of essential hypertension, a conception which is in line with the prevalent belief that hereditary predisposition is a key factor in this disease. Mendlowitz believes the deficient enzyme may be the recently discovered o-methyl-transferase. Since norepinephrine is the substance that stimulates vasoconstriction, and this hormone is degraded by o-methyl-transferase, the hypothesis seems impressive.

Pauling says:[8] "It is now known that a number of diseases are the result of some sort of abnormality involving enzymes, and that perhaps these diseases should be described as molecular diseases, resulting from the synthesis of enzymes of abnormal structure, which are not able to carry out in a proper way the work that the enzyme normally does. Sickle cell anemia was the first disease to be recognized as resulting from the gene-controlled synthesis of an abnormal molecule."

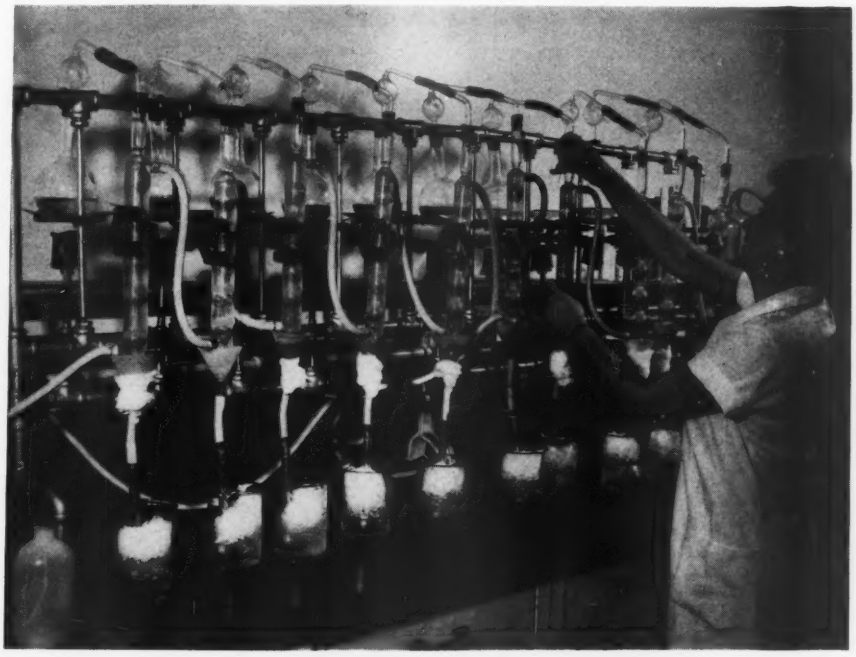
Pauling regards phenylketonuria, which leads to mental deficiency, as such a disease, "the result of a gene-controlled failure . . . to manufacture an effective enzyme that normally catalyzes the process of oxidation of phenylalanine to tyrosine. A score of diseases have so far been recognized as enzymic diseases. . . ." He goes on to say, "I foresee the day when many of these diseases will be treated by the use of artificial enzymes."

An ingenious application of enzymology began about 1940 in the laboratories devloping better methods of producing penicillin, where it was learned that certain bacteria produced an enzyme, penicillinase, which destroyed penicillin. Use of this enzyme became essential in testing for contamination of cultures. Later, the same enzyme was found valuable in clinical testing laboratories, where it was used to destroy the penicillin present in blood specimens taken from patients under penicillin treatment; this made it possible to culture the bloods for certain pathogenic bacteria such as are found in subacute bacterial endocarditis. Penicillinase was next used by Becker to destroy penicillin in guinea pigs, and later in patients suffering from penicillin allergy. For this purpose a purified product has been marketed as Neutrapen. Most recently Sallman and Streitfeld[2] of the University of Miami have reported efforts to discover a clinically practicable penicillinase inhibitor, to render penicillinase-producing bacteria susceptible to penicillin therapy. They have found trypsin, chymotrypsin and quinacrine active enough to warrant *in vivo* study.

Some realization of the overwhelming importance of enzymes and their apparently tremendous promise for future benefits to mankind leads us inevitably to deeper exploration of enzymology. We find that what

(*Continued on page 100*)

An important control measure of beer uniformity is the determination of its alcohol content. This bank of stills, with the distillate receivers in ice, is needed for precision in this analytical operation.



TGA Scientific Section Meeting 1958

The semi-annual meeting of the Scientific Section of the Toilet Goods Association took place at the Hotel Waldorf-Astoria on December 8. The officers of the section are F. J. Austin, honorary chairman. J. C. Ervin of the Procter & Gamble Co., chairman, W. W. Edman of Evans Research & Development Corp., vice-chairman, and H. D. Goulden, scientific director of the Toilet Goods Association, secretary. The papers presented at the meeting are abstracted below.

E. W. Daley of the Procter & Gamble Co. discussed a comparison of two methods of antiperspirant testing. His method uses the back of the subject and measures reduction in the number of color spots produced by later application of an anhydrous cream containing sodium carbonate and phenolphthalein. This contrasts with the Fredell and Read method which directly collects and weighs the perspiration produced in the axilla. The back test method is said to be more rapid and convenient and gives the same range of average results as the axillary procedure. With certain cream products which apparently form a surface coating on the skin, there is a large reduction of perspiration on the back but not in the axilla. Small panels do not give especially precise results with either method, but results are about the same with both and no better practicable method is as yet available.

The stability of alkyl sulfates to hydrolysis was determined by *R. R. Read and W. G. Fredell* of the Warner-Lambert Research Institute. They concluded that solutions of sodium lauryl sulfate are stable at room temperature, even at *p*H values as low as 3. Higher temperatures and acidity can result in breakdown up to 100 per cent in a few hours, or a shelf life shortened to only a few months.

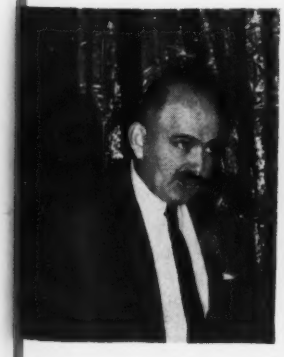
Robert E. Spinner of the Marketscope Research Company discussed converting laboratory concepts to the consumer market. The three common approaches used to evaluate product change and new product introduction are the use of the "expert" approach, the employee panel, and the laboratory approach. The expert approach uses one or a few persons who make all the final decisions as to product changes or new product introduction. The second approach in testing new product concepts uses small groups of untrained company personnel and the third or "laboratory approach" makes use of panels of adequate size and representativeness to obtain reliable and scientific data. The prime purpose of laboratory tests are to determine whether or not there is a difference in the test product apparent to the ultimate user after one exposure. There is also need, however, for extended use tests which permit the consumer to use the product many times under the conditions of use that follow a purchase. If the product has been developed and tested through each of the testing stages with the consumer in mind, the chances are that this testing cycle has developed a product which can gain consumer acceptance in the market.

The measurement of color impression was the subject of the talk by *Gabor B. Levy* of the Photovolt Corporation. Colorimetry is analysis *by* color while analysis *of* color involves quantitative evaluation in accordance with the human color-sense. The tristimulus system of color specification permits the objective and exact description of color by means of three numbers. Records of colors can thus be kept without the use of samples and the necessary instrumentation was briefly described. The limitations of the tristimulus system are physical and biological, due to individual variations in color perception. Since vision is basically a psychological process, psychology is an important factor in color perception.

The paper by *Otto K. Jacobi* of the Kolmar Research Center contributed an additional point to the problem of lipstick irritation. The lip is not stained uniformly by the so-called "kiss-proof lipstick." Only certain regions of the surface are stained since the applied lipstick mass reaches only the high spots. When excess mass is wiped off the lips, only the furrows and cracks in the lips contain lipstick material. Lips cannot be stained uniformly, despite repeated application of lipstick, the uniformity being apparent to the naked eye, but not on closer inspection. The penetration of stain amounts to only two-fifths of the stratum corneum thickness and the stain does not reach live tissue.

William O. Bracken of Hercules Powder Company gave a progress report on 18 materials such as polyols, fats, oils, and surfactants commonly used in toiletries with regard to weight and volume losses at room temperatures and at 120°F. when packed in high density polyethylene and polypropylene bottles. The two types of polyethylene studied were high density products, one with a nominal melt index of 3.5 and the other with an index of 0.2, and a commercial isotactic polypropylene.

An investigation was undertaken by *J. Calandra and J. H. Kay* of Bio-Test Labs. to evaluate in guinea pigs the effect of exposure to aerosol hair spray formulations. Two complete and two "partial" preparations, the latter based upon PVP and vehicle and on vehicle alone, were tested. The animals were exposed three times daily to high concentrations of the aerosol vapor for periods of from 45 to 90 days. Even under these drastic conditions, the hair sprays appeared to be innocuous.



FEMALE GENITO-URINARY INFECTIONS

BY BERNARD IDSON, PH.D.
RESEARCH DIRECTOR, JULIUS SCHMID, INC.

Despite the best efforts of modern hygiene to prevent them, and the development of a wide variety of treatments, female urogenital infections affecting the vagina, urethra and bladder are disconcerting problems for millions of women. Vaginitis is the most common disease of the female genital tract. Probably one-third of all women in the child-bearing age currently have one or more types of vaginal infection. The resulting physical irritations, esthetic objections and emotional irritabilities contribute immeasurably to psychosexual maladjustments in our society.

Sales of prescription drugs for the treatment of vaginitis are estimated at about nine million dollars at the manufacturer's level. Approximately 75 different products from at least 20 companies compete for this market and about 30 products control the bulk of sales (see chart, page 114). The local nature of treatment, coupled with the balloon-like character of the vaginal canal renders creams, jellies, suppositories and douches as the best dosage forms. For office treatment, powders for insufflation are common.

Like the mouth, nose and other body apertures, the lower female reproductive tract has its normal quota of microorganisms, including various species of bacteria, fungi, yeasts and protozoa. Ideally, there prevails among these microbes a balance which prevents any one species from multiplying disproportionately and attaining numbers and virulence sufficient to cause tissue damage. The balance is relatively delicate. It may be upset when broad-spectrum antibiotics used to combat infections elsewhere in the body eradicate many of the bacteria, leaving room for others, especially yeasts, to multiply freely, rather than be eliminated in the search for nutrition. Marital relation may play a role in disturbing microbial balance. The normal flora vary simply because of periodic hormonal changes, for example, in pregnancy when estrogen levels are particularly high. Actually, from birth to senility, a series of functional changes occur in the vagina which are associated primarily with variation in ovarian activity.

The female patient usually visits her physician because of leukorrhea. This is the term applied to any vaginal discharge other than blood. Almost invariably, leukorrhea is associated with some degree of irritation or itching of the genital structures and frequently there may be other local complaints such as painful irritation, painful copulation or irritation of the neighboring skin areas. Leukorrhea, it need hardly be said, is a symptom of an underlying basic cause and not a disease entity. Not all vaginitis is associated with a copious discharge, and not all leukorrheas result from vaginitis.

Vaginitis can most conveniently be divided into those of bacterial, protozoal and yeast fungal origin. Bacterial vaginitis is usually due to streptococcus, staphylococcus or lactobacillus. The lack of a single responsible bacterial pathogen has led to the term "nonspecific vaginitis." Recently, it has been claimed that the bulk of nonspecific infections stems from a newly discovered bacteria, *Hemophilus vaginalis*. Considerable data support this claim of a specific organism responsible for bacterial vaginitis. Sterisil (Warner-Chilcott) has been promoted largely on its action against *H. Vaginalis*. Actually, most bacterial infections occur concurrently with other pathogens.

It is estimated that about 25 per cent of vaginitis is due to mixed infections.

The two most prevalent types of vaginitis are those due to the protozoa, *Trichomonas vaginalis*, causing trichomoniasis, and the yeast, *Candida albicans*, causing moniliasis. Trichomonal vaginitis is apparently the form most commonly encountered, but the incidence of moniliasis is not far behind, and in pregnant women is certainly more common.

The chief manifestation of trichomoniasis is leukorrhea. The discharge may be rather thin and milky, but often it is very thick and whitish or yellowish white. The mucuous membrane of the vagina is reddened and inflamed. There is still much uncertainty as to the source of the infection. There is increasing evidence that the organisms are transmitted through coitus, as they are often found in the male urethra. However, venereal transmission cannot be the sole cause. The incidence of trichomoniasis in women of all ages is variously reported at 20 to 80 per cent. Most cases are mild, but about 10 to 15 per cent of cases are extremely resistant.

Moniliasis, a mycotic vaginitis, occurs in at least one-third of pregnant women and in about 10 per cent of nonpregnant females. The patient usually notices a genital itching before leukorrhea. The discharge has a characteristic yellow to white color, cheesy and rather dry. The vaginal mucosa is reddened, swollen and covered with flaky patches. The organisms responsible are fungi of the yeast group.

The main predisposing factor is a high vaginal carbohydrate content. The glycogen content of the vaginal epithelium increases markedly during pregnancy and further increases as gestation progresses. This is ascribed to a lowered renal threshold level and some diminution in glucose tolerance. These facts account for the much higher incidence of vaginal fungal infections in pregnant women.

Yeastlike fungi occur most often in association with the normal acidophilic organisms of the vagina, particularly Doderlein's bacilli (indistinguishable bacteriologically from lactobacilli). The latter, by decreasing the *p*H of the vaginal secretion, maintain an environment detrimental to the growth of most bacteria but highly favorable for their own maintenance and for the growth of candida organisms.

A relatively new cause for moniliasis, especially in nonpregnant women, has been the use of broad-spectrum antibiotics. Vaginal moniliasis may occur in as many as 75 per cent of patients receiving local vaginal therapy with tetracyclines for the treatment of other types of vaginitis and cervicitis. The addition of fungistatic agents such as Nystatin or the methyl or propyl esters of parahydroxybenzoic acid has been found to reduce markedly the incidence of this complication.

Treatment of the vaginitis depends on the experience of the physician. He may prescribe preparations designed for a particular vaginitis, such as Triple Sulfa Cream (Ortho) for bacterial vaginitis, Vagisec (Schmid) for trichomoniasis or Mycostatin (Squibb) for moniliasis. He would do so either because he trusts his diagnostic judgment as to the specific infection, or on the basis of an actual culture of the invading organism. However, studies of prescription volume show that the largest sales are enjoyed by those drugs designed and advertised for treatment of all three types of vaginitis. A recent survey showed that the two largest sellers are Floraquin (Searle), which averaged slightly over 20 per cent of all vaginitis prescriptions, and AVC Improved (National Drug), which accounted for over 10 per cent of the prescriptions sold. These two are "over-all" vaginitis drugs. Behind these in sales come Milibis (Winthrop), Tricofuron (Eaton), Mycostatin (Squibb), Aci-Jel (Ortho), Vagisec (Schmid), Nylmerate (Holland-Rantos), Sterisil (Warner-Chilcott) and Gentia Jel (Westwood). All of the foregoing, with the exception of Gentia Jel, Vagisec and Mycostatin are recommended for more than one vaginitis, accounting for well over 80 per cent of prescriptions.

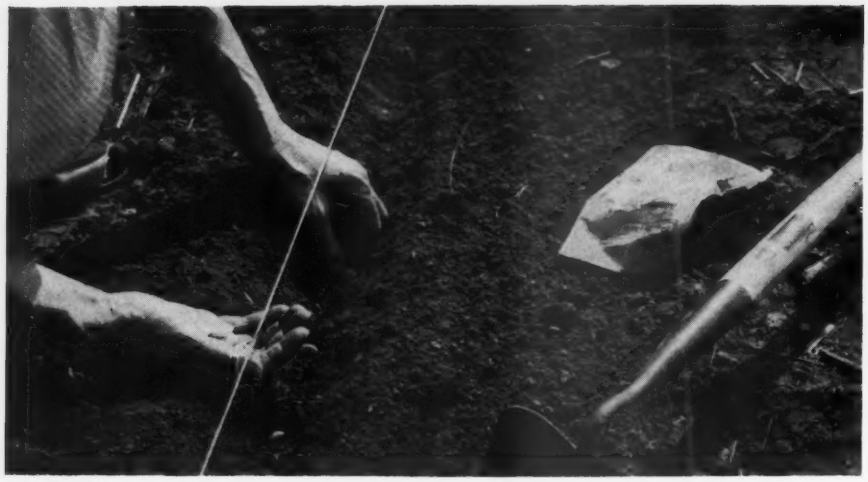
In questionnaires to doctors, surveys showed that for mixed bacterial or non-specific infections, the preferences are for AVC-Improved (National Drug), Triple Sulfa Cream (Ortho), Sterisil (Warner) and Floraquin (Searle); for trichomoniasis, Vagisec (Schmid) and Floraquin (Searle) are most prescribed. Mycostatin (Squibb) is the leader in the moniliasis field.

As to dosage forms, physicians seem to prefer inserts (tablets) or suppositories, with douches and jelly next. This might be interpreted as due to convenience of use and to elimination of office treatment. Oral treatment has met with varying success. Tritheon (Ortho) has been advanced as an oral treatment for trichomoniasis. There is certainly a need to treat males who may transmit the disease to their wives. The results with Tritheon have, however, been equivocal. Oral Mycostatin (Squibb) has been quite effective in suppressing growth of enteric fungi which may ultimately invade the vagina.

Vaginal use of broad-spectrum antibiotics does not appear to have made appreciable inroads. Of the roughly nine million dollar sales at the manufacturer's level, less than one-half million is credited to the antibacterial antibiotics. There is concern about overgrowth of monilia and possible development of resistant bacterial strains.

The simplest mode of treatment of nonspecific vaginitis is to increase the vaginal acidity. A simple water-soluble acid jelly, such as Aci-Jel (ortho) is often quite effective. In cases which fail to respond, the local use of a sulfonamide cream such as Triple-Sulfa Cream (Ortho) and Gantrisin (Roche), or of antibiotic suppositories such as Cortril (Pfizer), is usually effective. Vacid (Fesler) is a suppository containing polyacrylic cationic exchange resin, which exchanges hydrogen for sodium ions, thus lowering the

(Continued on page 115)



GENDREAU PHOTO

BARRIER CREAMS*

BY MARVIN K. COOK CONSULTING CHEMIST

Protective or barrier creams are those hand preparations which provide resistance to various types of soil and irritants encountered in the home and in industry. There is unquestionably a growing interest in products that offer reasonably good barrier action while simultaneously possessing cosmetic elegance. Today, an unusually large variety of substances are available to the formulator, which exhibit interesting and useful properties as barrier agents.

The basic type of barrier cream is a modified vanishing cream and, in addition to the customary stearic acid emulsion, film formers and water repellants are usually incorporated. Often an excess of surfactant is built into the formulation to facilitate removal upon washing with soap and water. Fundamentally, protective hand creams fall within two general categories, water-repellant and oil-repellant. The water-repellant creams simply act as barriers against water and therefore provide protection against irritating agents dissolved in water. On the other hand, the oil-repellant products protect against oil and oil-based irritants.

That the protective action of modified stearic acid creams is well known, is evinced by the use of ordinary brushless shaving cream as hand protectors in some segments of the printing trades. This offers resistance to the nearly permanent ingraining of the skin by inks, and is achieved by merely filling the skin surfaces and crevices with a thin stearic acid film. Furthermore, the film is dry and non-greasy.

The incorporation of ink solvents such as deodorized kerosene and isopropyl myristate would serve advantageously in formulating protective creams or cleansing creams for the graphic arts industry. The dehydrating and defatting action of some washup solvents (not to mention irritation), the marked staining properties of most printing inks and the drying action of certain paper stock on the skin suggest

*From a forthcoming book by J. Kalish and M. K. Cook.

the many possibilities in developing effective barrier creams in specific areas.

Protection requirements may extend to other portions of the body, particularly for military use, for instance, toxic vesicants and flash burns from high explosives. Formulation and evaluation generally require highly specialized training and knowledge. In steel mills and on shipboard where high temperature heat waves of short duration are encountered, flash burn protectants based on earth oxides and silicones have proved useful.

An efficient, all-purpose barrier cream is virtually non-existant; there is no single product that provides absolute protection against every type of soil and irritant. The range from the do-it-yourself amateur house painter to the handler of hazardous industrial products is indeed vast. In fact, it may be considered an achievement if a particular formulation designed to resist a specific irritant can even approach maximum efficiency under all conditions.

There are many barrier agents and the end use is, of course, the determining factor in proper selection. A simple but rather effective water repellant is zinc stearate. The silicone oils offer a rather wide range of protection, particularly when combined with other barrier agents. The relative inertness of the silicones to many organic and inorganic compounds, their efficacy at low concentrations and lack of interference with normal hand perspiration are valuable attributes.

One of the most important characteristics of a protective cream is its ability to form a resistant film that would be reasonably durable, flexible, comfortable and effective. Greasy, tacky or slick films are obviously not desirable. After use, the barrier cream should be easily removable, preferably with soap and water.

Numerous substances are capable of forming films. New plastics and synthetic rubber film formers would seem to offer unusual possibilities to the imaginative and creative formulator. Of particular interest are the polyvinyl acetate emulsions and butadiene-styrene latices—assuming, of course, an absence of skin-irritating properties.

A general list of applicable film-forming agents and barriers would comprise the following:

1 VEGETABLE GUMS
- Tragacanth
- Karaya
- Quince seed
- Irish moss
- Alginates
- Guar

2 CELLULOSE DERIVATIVES
- Methylcellulose
- Sodium carboxymethylcellulose
- Nitrocellulose
- Cellulose acetate
- Cellulose acetate butyrate
- Ethylcellulose

3 POLYMERS
- Silicone oils
- Polyvinyl alcohol
- Polyvinyl pyrrolidone
- Polyvinyl acetate
- Carbopol
- Terpene polymers
- High molecular weight ethylene oxide polymers
- Butadiene-styrene latices

4 INORGANIC COMPOUNDS
- Sodium silicate
- Colloidal magnesium aluminum silicate
- Hydrated magnesium aluminum silicate
- Hydrous magnesium silicate

5 NATURAL AND HYDROCARBON WAXES AND OILS
- Beeswax
- Paraffin
- Ozokerite
- Mineral oil
- Petrolatum
- Lanolin
- Polyoxyalkylene lanolins

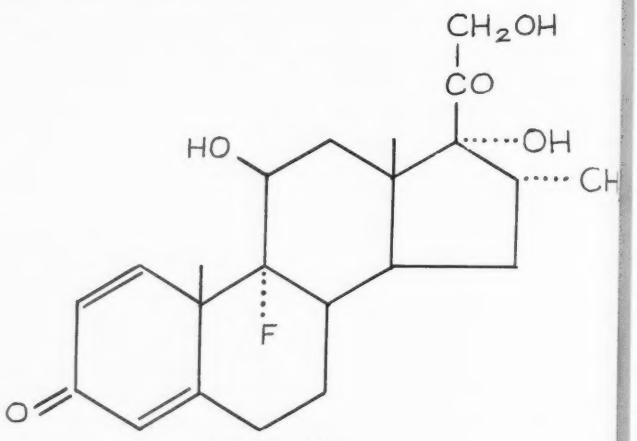
6 FATTY ACIDS, ESTERS, ALCOHOLS AND SOAPS
- Stearic acid
- Metallic stearates
- Glyceryl monostearate
- Polyethylene glycol fatty acid esters
- Cetyl alcohol
- Stearyl alcohol
- Butyl stearate
- Isopropyl stearate
- Isopropyl palmitate
- Isopropyl myristate
- Spermaceti

1. Vegetable Gums. Natural gums have a multiple function in protective creams. They provide stability, good skin feel and, as film formers, offer a moderate degree of protection. In certain formulations, in conjunction with other barrier agents, outstanding skin-protective properties have been noted. All these gums are hydrophilic and the films they form are therefore primarily oil and grease resistant.

2. Cellulose Derivatives. These synthetics have the same basic application as vegetable gums. They are excellent film formers and the films can be plasticized for special effects. Some films, such as those derived from methylcellulose combine easily with gum arabic, karaya, alginates, polyvinyl alcohol and starch. This compatibility allows for wide modification for specific end use. *(Continued on page 110)*

GENDREAU PHOTO

ANTI-INFLAMMATORY STEROIDS



DEXAMETHASONE

A conference reviewing the development of the anti-inflammatory steroids and their use in treating anti-inflammatory diseases was jointly sponsored in December by Merck Sharp & Dohme Research Laboratories, Schering Corporation and the New York Academy of Sciences. The conference was held at the Barbizon-Plaza Hotel in New York City, and the over-all chairman was Joseph J. Bunim of Johns Hopkins University School of Medicine and the National Institute of Arthritis and Metabolic Disease. Session chairmen were J. J. Bunim and Russell L. Cecil of Cornell University Medical College, Edward C. Kendall and Philip S. Hench who shared the Nobel Prize, with T. Reichstein, for the isolation, synthesis and application of cortisone to the treatment of rheumatoid arthritis.

Over the last ten years synthetic modifications of cortizone have included biologically active and inactive analogs in almost every position in the steroid nucleus. Modifications with anti-inflammatory activity, according to *L. H. Sarett*, include hydrocortisone, the Δ^1-steroids, 9-halogen, 6α-methyl, $\Delta^{1,4,6}$-triene, 6α-fluoro, 12α-halo, 2α-methyl, 16α-hydroxy, 21-desoxy, and 16-methyl steroids. Compounds which are noteworthy for their lowered activity are 6β-methyl, 9α-methyl and 11α-methyl.

From the medical and biological viewpoints the goal of this synthetic effort has been to achieve a "pure" anti-inflammatory activity. In aiming at this objective an attempt has been made to associate structural features with individual aspects of the biological spectrum of the anti-inflammatory steroids. So far enough data has been accumulated only to attempt one such correlation with a degree of confidence. This is embodied in the construction of the hypothetical anti-inflammatory receptor site at the molecular level. The main features of this receptor site appear to involve a three-point combination with the β-face of the steroid molecule.

Additions of a methyl group in various positions of the steroid molecule have had unpredictable and variable effects on the activity of the parent corticoid, ranging from complete loss of activity to a marked increase in electrolyte retention. When the synthesis of 16-methylcorticoids was undertaken, according to *E. Oliveto*, there was no way of predicting activity. The 16 alpha and 16 beta derivatives were made by reactions based upon those discovered by Marker and Crooks in 1942 and by Wettstein in 1944.

The potencies of dexamethasone and other 16 methyl steroids have been determined by *R. H. Silber* in both liver glycogen deposition and granuloma inhibition tests. Dexamethasone has been found to be the most potent steroid; it was about 20 times as potent as hydrocortisone in glycogen deposition and 200 times as potent in granuloma inhibition.

Although two of the steroids had a fluorine at the 9 position, they did not cause sodium retention in adrenalectomized rats. Thus, the introduction of the 16α-methyl function has not only led to an increase in anti-inflammatory potency but has also eliminated the sodium retaining property expected of a 9-fluorosteroid.

In vitro studies with human plasma showed that the introduction of the methyl group at the 16α position influenced the binding of the steroid to plasma protein and also the stability of the side chain.

Some of the routine methods employed in the study of new synthetic steroids were discussed briefly by *S. Tolksdorf*. Anti-inflammatory activity, hormonal activity, mineralocorticoid activity and metabolic effects were studied.

The effect of α- and β-methylation at carbon 16 on biological activity has been studied in 11-desoxy, 17 hydroxy steroids, in 11-keto steroids and in 9α-fluoro, 11-hydroxy steroids.

The rate controlling reaction in corticosteroid degradation by liver, according to *G. M. Tomkins*, is the saturation of the 4, 5 double bond of the A ring which may be accomplished by two separate enzymatic means.

Both of these reactions are TPNH-dependent and the concentration of intracellular TPNH has been found to limit the rate of steroid inactivation by these enzymes in crude liver extracts. Alterations in the level of enzymes involved in TPNH production can

change the rate of steroid inactivation.

Since it has also been shown that the rate of corticoid biogenesis is regulated by the adrenal TPNH concentration, a control mechanism exists which could serve to maintain blood corticoid levels constant in a variety of situations.

Conversely, corticosteroid degradation by this pathway can increase the amount of TPN at the expense of TPNH and thereby enhance the rate of TPN-dependent oxidations.

Comparative studies have been made by *R. E. Peterson*, in man, of the metabolism of the naturally occurring adrenocortical steroids: cortisol, corticosterone, and aldosterone. These studies have included measurements of the rate of biotransformation and the rate of synthesis of the steroids. Studies have been carried out on normal subjects both before and after treatment with drugs or various experimental procedures designed to alter adrenal function and the metabolism of the steroids. Studies were also carried out on patients with various diseases.

An important advance in the field of corticotherapy, according to *G. W. Liddle*, has been the advent of several new synthetic steroids which, compared with cortisone itself, exhibit enhanced anti-inflammatory potency without commensurate enhancement of electrolyte-regulating potency.

Corticosteroids may cause Na ion *loss* by either of two mechanisms: by increasing glomerular filtration rate or by "aldosterone antagonism."

Introduction of a halogen atom in 9α-position of the steroid nucleus results in general enhancement of biologic activity, especially electrolyte-regulating activity; 1,2-dehydrogenation enhances anti-inflammatory activity but slightly diminishes electrolyte-regulating activity; 2α-methylation markedly increases electrolyte-regulating potency of 11β-hydroxy-corticosteroids while altering only slightly their anti-inflammatory and related activities; biologic consequences of 6α-methylation are so variable from one steroid to another that generalization is impossible; 16α-hydroxylation diminishes biologic activity generally, especially electrolyte-regulating activity; 16α-methylation markedly diminishes electrolyte-regulating activity and slightly increases anti-inflammatory activity; effects of introducing multiple structural alterations are often multiplicative, so that 9α-fluoro-Δ^1 - 16α - methyl - hydrocortisone (dexamethasone) is the most potent anti-inflammatory steroid yet described, whereas its electrolyte-regulating activity is too slight and inconsistent to be readily measurable.

The overall results from systemic cortisone and hydrocortisone therapy in rheumatoid arthritis indicate that the hormones will provide adequate control of the disease, for long periods, in more than one-half of patients treated. Hormonal side reactions prohibiting the use of effective doses, or the failure to achieve or maintain adequate improvement, have been the most frequent reasons for inferior results.

E. W. Boland appraised the relative merits and deficiencies of a number of analogs that have been tested clinically in rheumatoid arthritic patients. These include: Hydrocortisone, prednisone, prednisolone, 9-alpha fluoroprednisolone, triamcinolone, 6-alpha methyl prednisolone and, recently, several 16 alpha and beta methyl derivatives of hydrocortisone and cortisone.

Clinical studies with one of the 16-methylated analogs — dexamethasone — have been conducted for nearly one year. The milligram antirheumatic potency of this compound has been determined to be about seven times that of prednisolone, and the steroid is highly effective in suppressing the manifestations of rheumatoid arthritis when it is administered in remarkably small doses.

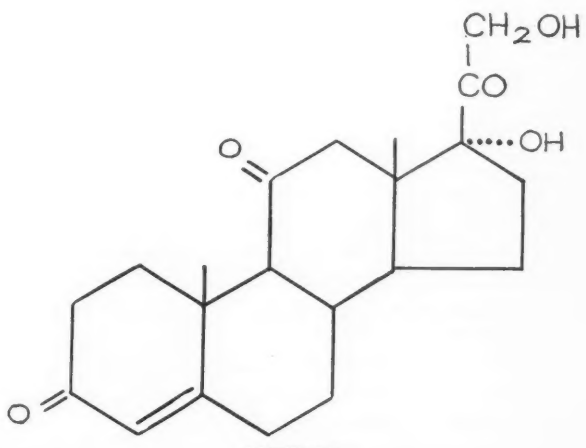
Ever since the introduction of corticotrophin and cortisone as therapeutic agents for the management of diseases of allergy, there has been much controversy as to their real value and potential harm.

A short course of treatment followed by remission, maintained by adequate conventional therapy is the ideal and may frequently be achieved in suitable patients, according to *B. Rose, A Knight and E. McGarry*.

In general, if an underlying disease such as latent hypertension, diabetes mellitus or osteoporosis be present, these may be accentuated by continued hormone treatment. On the other hand, even after as long as eight or nine years continued administration, no evidence of any alteration in the physical status of others can be shown. Both improvement in general health such as increased resistance to infections or the reverse have been observed.

The revolution in hematologic therapy, according to *W. Dameshek*, brought about by the corticosteroids is startling. They have become an essential item in the management of such diverse disorders as leukemia, auto-immune hemolytic anemia, idiopathic

(*Continued on page 120*)



CORTISONE

ALLANTOIN AND ALUMINUM DERIVATIVES IN DERMATOLOGICAL APPLICATIONS

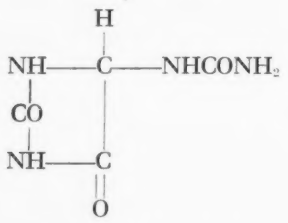
BY IRWIN I. LUBOWE, M.D., F.A.C.A., AND S. B. MECCA

DEPARTMENT OF DERMATOLOGY, NEW YORK MEDICAL COLLEGE AND METROPOLITAN HOSPITAL CENTER, NEW YORK CITY

CHEMICAL DIRECTOR SCHUYLKILL CHEMICAL COMPANY, PHILADELPHIA, PENNA.

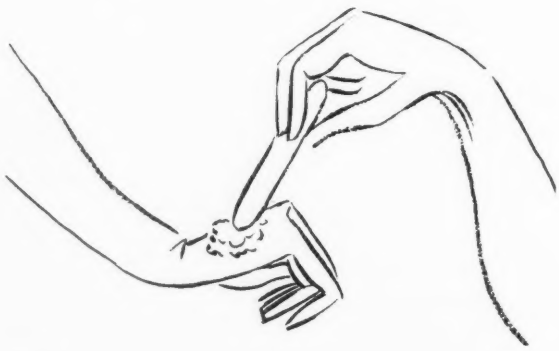
Over fifty years ago, allantoin was introduced to the medical profession for the effective treatment of many dermatological affections. Since its recent advent into cosmetic formulations[12] it is being given a well-deserved place of prominence as an invaluable adjunct in specific types of preparations because of its desirable attributes. Allantoin is today recognized and accepted by the medical and related professions for its effective anti-irritant, keratolytic and healing action clinically proven for many years.

This compound has unusual chemical and physical properties which, no doubt, are responsible for its unique therapeutic activity. To review briefly, allantoin is a uric acid derivative[11] chemically known as glyoxyl-diureide or 6-ureidohydantoin. It was first synthesized by Wohler and Liebig in 1838, by Schliper in 1848 and by Neubauer in 1856. It has been prepared by the alkaline oxidation of uric acid as well as by reacting glyoxylic acid with urea. Its structural formula can be expressed as



Allantoin is a bland, stable, odorless white powder soluble in 170 parts cold water and very soluble in hot water; also soluble in 500 parts isopropyl or ethyl alcohol and insoluble in organic solvents. It is soluble with subsequent decomposition in sodium or potassium hydroxide solutions. Its molecular weight is 158.08 and the *p*H of a saturated (0.6 per cent) aqueous solution is approximately 6. Its melting point is 228 to 234° C. with decomposition.

Many scientific references and papers have been published demonstrating the therapeutic properties of allantoin, particularly as a topical agent. It has been observed that allantoin stimulates healthy granulation of tissues that are ulcerative, fissured and in which keratinization has been slowed. Although it does not possess any germicidal nor antiseptic properties, it debrides necrotic tissue and acts as a cleansing agent.



Berthelot and Bertrand[1] have suggested that favorable local cutaneous action is due to the local leucocytic effect of allantoin. No toxic reaction, either as a primary irritant or as a sensitizing agent, has been reported in any of the literature. In contrast, it has been mentioned from time to time that urea causes local discomfort and irritation when used in the treatment of various dermatological affections. Brush and Lam[3] have reported observations of urea inhibiting wound healing.

Robinson[15] states that after a few topical treatments with allantoin in ulcer therapy, small areas of shining pinkish granulation tissue can be seen forming in the wound. Comunale[5] reports the successful treatment of osteomyelitis with allantoin ointment, while Rice[14] mentions the therapeutic effectiveness of allantoin on diabetic ulcers. LeVan, *et al.*[10] describe a combination of allantoin with silicones, a bacteriocidal

agent such as hexachlorophene, plus menthol and camphor as being helpful in alleviating subacute and chronic housewives' eczema, and other types of contact dermatitis of the hands. We have found allantoin to be an effective epithelial stimulant and detoxifying agent.

Flesch[7] observed that saturated solutions of allantoin demonstrated marked denaturation or dispersion of epidermal horny material. This dispersion is observed as a two to threefold increase of reactive sulfhydryl over the aqueous suspensions of epidermal tissues. Furthermore when the saturated solution of allantoin was diluted with water to 25 per cent of its original concentration,[6] its protein dispersing effect remained the same as that of the saturated solution.

As a result of the above and subsequent studies, it can be surmised that allantoin has a softening and dispersing effect on hyperkeratotic epidermal tissues in dermatoses. Further, a commercial product containing allantoin in combination with coal-tar derivatives in a lotion proved effective in the topical treatment of psoriatic lesions and eruptions. Clinical observations on this lotion were recently reported by Bleiberg[2] and by Clyman[4] in a conference at the New York Academy of Sciences.

In view of the protein-dispersing effect of allantoin, its further effectiveness can be evaluated in the treatment of other dermatological entities presenting parakeratosis and hyperkeratosis as observed in seborrhoic dermatitis and exfoliating dermatoses.

Allantoin is applied by means of solution, emulsion, powder or ointment form, alone or in combination with other therapeutic agents. Its full activity is observed whether in solution, emulsion, suspension using oils, washes or in a dry form. The suggested therapeutically active concentrations are from 0.01 to 2 per cent. Effective management of diaper dermatitis with an allantoin talc has been reported by Kaessler.[9]

During the past year, a new group of allantoin complexes and compounds have been developed, namely, the aluminum allantoinates.[13] These salts are stable, effective chemical compounds of allantoin. They are a combination of the astringent and bacteriostatic action of the aluminum with the above-described activities of allantoin. Thus, in one compound there is an often sought therapeutic balance of healing, cleansing, bacteriostatic, and astringent activity coupled with soothing, anti-irritant properties. At this writing two of these compounds are commercially available, namely, Aluminum Chlorhydroxy Allantoinate and Aluminum Dihydroxy Allantoinate, from Schuylkill Chemical Company.

The molecular formula for aluminum chlorhydroxy allantoinate is $Al(OH)_4ClC_4H_5N_4O_3$. It is soluble in about 55 parts water and in 200 parts alcohol. It is very soluble in hot water. The *p*H of a saturated solution (1.7 per cent) is approximately 4.7.

The molecular formula for aluminum dihydroxy allantoinate is $Al(OH)_2C_4H_5N_4O_3$. It is insoluble in water and alcohol. It has both acid and alkali (ammonia) consuming properties. The *p*H of a 4 per cent suspension is approximately 7.5.

We have found aluminum chlorhydroxy allantoinate to be an effective deordorant, mild astringent, anti-irritant and healing stimulant. A keratolytic and bacteriostatic action was also observed. Aluminum chlorhydroxy allantoinate can be used singly (0.25 per cent) in deodorant preparations or as an additive (0.25 per cent) to antiperspirant-deodorant formulations. Such antiperspirant-deodorant preparations are easily tolerated by individuals whose history indicates they are generally prone to irritation and reaction when using antiperspirants. It was most interesting to note that it actually considerably reduced the irritant potential of antiperspirant-deodorant preparations.

Clinical evaluations of aluminum chlorhydroxy allantoinate involved lotions containing 2 to 4 per cent concentrations of this material in a triethanolamine emulsion for the treatment of acne vulgaris of the papular pustular type. These formulations did not contain any of the usual keratolytic agents and other compounds, such as sulfur, salicylic acid, or resorcinol and its derivatives, generally used in acne formulations. In a large percentage of cases, the acne lesions dried, and relief of itching, erythema and comedomes were observed. The lotion was cosmetically elegant, non-odorous and absorbed by the skin, preventing staining of the skin or bed-clothes. It would be interesting to observe the action of aluminum chlorhydroxy allantoinate in combination with colloidal sulfur, resorcinol, salicylic acid and hexachlorophene as new acne therapeutic modalities.

We have also been testing the deodorant effect of aluminum chlorhydroxy allantoinate (0.25 per cent) in a series of 25 patients, and have observed it to be an effective agent for complete inhibition of odor formation for 24 hours after application.

Flesch[8] has also demonstrated *in vitro* that 0.2 per cent concentrations of aluminnum chlorhydroxy allantoinate will inhibit odor formation and bacterial decomposition of pulverized human epidermal scales. He further observed[7] that similar solutions demon-

(Continued on page 117)

FRAGRANT AEROSOLS
Ancient and Modern*

BY E. R. VAN LIEW AND VICTOR D. GIACOMO
GIVAUDAN-DELAWANNA, INCORPORATED

Regardless of what agreements or disagreements authorities may have concerning our prehistoric ancestors, on one point there appears to be no doubt whatever: man's sense of smell is a means of self-preservation. But, it took man no time at all to discover that his olefactory sense also offers pleasures.

The early cave man was primarily carnivorous and his chief activity was to supply meat for the family and the tribe. Whether he hunted with stone, spear or bow and arrow, his quarry was good for just so many meals, and he soon learned that to eat meat that smelled unappetizing invariably resulted in a bellyache, or worse.

Since the pleasant and the unpleasant are inextricably bound together, it was inevitable that agreeable smells should be a source of enjoyment, even as the disagreeable ones were the opposite. Just when man began to appreciate the fragrance of wild flowers is difficult to say. We know, however, from the earliest histories of China and India and, of course, from the Old Testament, that man took only a few hundred years to realize that certain pleasant-smelling odoriferous substances could be extracted from vegetable and animal matter and used to perfume an object or a human being, by direct application as well as by burning.

Religious Use

Much has been written concerning the use of aromatics in incense and unguents, especially in connection with ancient religious rites. From the worship of the gods, the use of pleasing fragrances naturally was taken up by royalty, the wealthy families and the priesthood.

Too often we think of these usages as restricted to the major civilizations of their day—ancient Egypt, Greece, Persia and Rome. It is interesting to note, however, that some twelve hundred years before Christ, the Children of Israel, whom we picture as a bedraggled and downtrodden mob, wallowing in brickmakers' clay and starved to the point of exhaustion, placed considerable emphasis on the use of aromatics in their worship of Jehovah. We are informed that after they were released from their bondage and wandered for 40 years in the desert, every family was well equipped with censers and perfumes to carry on their worship of Jehovah in the proper manner. The Book of Numbers goes into considerable detail on this subject indicating that certainly the head of each "family" had a censer.

The censers as used in the temples produced what might be called the first aerosol method of perfuming the atmosphere, since incense consists of small solid particles suspended in air. Furthermore, we know that the Chinese, from the beginning of the Shang Dynasty, burned incense in their temples and in the home shrines reserved for ancestor worship.

It may be unkind, but it is probably correct to assume that, consciously or unconsciously, the worshippers were covering up their own body odors and those of their sacrificial animals in an effort to make their prayers more acceptable to the deity.

Middle Ages

Not too much is known of the use of perfume during this period. The educational curve took a sharp drop and for several hundred years those who knew how to write devoted most of their time to the laborious longhand reproduction of religious and philosophical works. Personal deodorization, how-

COURTESY DOROTHY GRAY

*Presented at the 45th Annual Meeting of the Chemical Specialties Manufacturers Association, Inc., December 1958.

ever, is mentioned in connection with the great crusades. Since the Knights in Armor employed certain inhuman means of insuring the fidelity of their wives during their prolonged stays in the Holy Land, the Frankish, British, and Germanic ladies had to resort to effective deodorants to be able to live with themselves while their gentlemen were in distant lands slaughtering the Saracen (who was culturally far ahead of his European foes).

It is known, moreover, that during what we may call the dawn of modern medicine certain aromatic herbs were used and burned for their therapeutic value. This is the second stage of aerosol development.

Modern Times

Some historians may disagree with this designation for the beginning of the Age of Elegance, which attained its summit in the days of King Louis XIV of France when gentlemen and ladies were perfumed equally and profusely. This was immediately followed by the Age of Foppery after Napoleon's reign. Theaters were designed to separate the perfumed gentility from the unwashed peasant; at the first production of Hamlet the common man was segregated in the area known as the pit, which has evolved to the modern orchestra. In the days of Napoleon one of the highlights of the intermission was fumigation of the theater. Perfume bullets, not *perfumed* bullets, were shot from conventional firearms to permeate the atmosphere with the odor of lilac, rose and carnation for the benefit of the guests. We may look upon this as the third phase of the development of the aerosol.

Our Times

Those who attended silent movies may remember that the poorly ventilated theaters had a "typical movie odor." This was a combination of the odor of damp clothing, humanity and management's effort to overcome these through the use of theater sprays. These were usually made of aqueous solutions of inexpensive perfume compounds premixed in turkey red oil and sprayed throughout the premises with the help of a spray gun and a strong back. The perfumes were cheap, heavy reproductions of rose, newmown hay and clover. Despite their power and residual characteristics, however, they never quite succeeded in covering the fatty odor of the water-soluble agent, which could still be smelled.

Were we subjected to such odors, we would quickly express our objection to the theater management. Today's public is conscious of upgrading odor just as it is of the refrigerator, the automobile and stereophonic high fidelity.

Not too long ago certain theaters introduced crude air conditioning systems that involved passing outside air over pans of cold water and blowing it into the theater. There was an attempt to incorporate water-soluble perfumes in that water, so as to perfume the inside of the theater. This may be called the fourth step in aerosol development, but it was relatively short-lived because of the swift advances in modern air conditioning.

It is not surprising, in view of this formidable background of customs, that we who live in the year 1958 provide such a ready market for the little gadget whose 10th anniversary is being celebrated currently. Our extreme consciousness of all unpleasant odors has resulted in the invention of personal deodorants, the acceptance of daily bathing as a must, the installation of exhaust fans in our kitchens and the like, and we in the United States are ready and willing to perfume, deodorize and freshen the air we breathe.

Let us briefly review the most important successes of our gadget. Of these, the room deodorant would have been a complete failure had it not been for fragrance, whether used in the home, in the theater, or wherever large numbers of people gather. Certain germicides can be added to enhance the functionality of this spray. Our gadget has even helped the weekly poker groups, for the accumulation of smoke in my lady's living room is no longer a valid cause for nagging friend husband when he announces that the boys are coming over for an evening of stud. With three squirts she can make her home livable the following morning.

The next important functional item is the aerosol insecticide, and anyone eager to know which of these sell best will find that they are the ones having the most pleasant odors. Battling a dozen ferocious mosquitos on a summer night is an aggravating experience. Disposing of this pest by the aerosol method is easy and effective, but the humans who must then

(*Continued on page 122*)

COURTESY TUVACHE INC.

COURTESY HELENA RUBINSTEIN

MEASURING SKIN RESPIRATION

BY HENRY GOLDSCHMIEDT, Ph.D. CONSULTANT

A Warburg respirometer, which is used to determine precisely the respiratory rate of micro-organisms and tissue cells. Measurements are determined by precise manometric readings of gas pressure changes.

COURTESY WALLERSTEIN CO.

It is well known that respiration takes place in the skin. In fact, once the skin ceases to breathe, it dies. The rate of skin respiration is greater in young people than in adults. Heat, cold and other physical influences may increase or decrease skin respiration. In cold weather the skin respiration slows down; it increases in hot weather. Chemical materials also may increase or decrease the respiration rate. This means that some cosmetics, rather than stimulating the skin as intended, actually slow down skin respiration, acting as inhibitors. Others are effective activators, having a stimulating effect on the skin's respiration rate.

So far, no method exists to study the influence of a medication, chemical or tissue preparation on the human skin *in situ* (in the living body). We must therefore study this influence only in living tissue removed from the body. With the method described below, it is possible to ascertain if skin respiration is increased or decreased, if the material tested is an inhibitor activator of the skin.

We have found that each material has a specific oxygen consumption. The following tables will show, for example, that domestic hops have a different oxygen consumption from European hops. This makes identification of a hops sample easy with the Warburg apparatus. The same is the case with perfumes or some organ extracts used in cosmetics.

Amersbach, Nutini and Cook found the measurement of skin respiration to be a valuable dermatological tool. In cases of vitamin deficiency they found that the rate of skin respiration decreases. Preservatives and antiseptics also depress skin respiration, as do fatty acids.

Adams demonstrated a decline in the respiration of rat or mouse skin with increasing age. Brotzge and Loeffler confirmed these results.

Walter and Amersbach investigated the respiratory rate of human skin, and results indicated that the oxygen consumption of skin is lower in older than in younger subjects.

Weiss used the manometric method for testing the activity of tissue extracts. The oxygen consumption or the increase of tissue respiration was used for standardization. Weiss used as substrate mice ascites or rat liver homogenates.

Cook, Kreke and Nutini found that yeast contains factors that stimulate the respiration of rat skin and rat liver.

We used the Bronwille apparatus in a modification of the direct Warburg method. Forty milligrams of sliced skin from baby mice were used as a substrate, since this tissue is nearly hairless with no fat deposit and, therefore, is similar to human skin. Consequently, the reactions shown in tests made with baby mice skin are similar to those of human skin, which makes standardization possible. By such tests it can be established whether the material tested is an inhibitor of skin respiration or an activator, and to what degree.

The pieces of tissue are used as soon as possible after removal and are kept at body temperature in Ringer solution until placed in the Warburg apparatus.

In the outer well of each vessel we put 2.0 ml. skin slices homogenized in Krebs Ringer phosphate dextrose solution. The inner well of the vessel was filled with a 20 per cent potassium hydroxide solution. In the sidearm we put 0.2 ml. of the material to be tested for measurement of skin respiration.

The manometers were shaken at a rate of 120 oscillations per minute for a two-hour respiration period at 37.5° C. At intervals of 10 minutes the readings of the manometer were taken, for 60 to 90 minutes. (*Continued on page 118*)

Packaging and Selling

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The Professional Package Designer Comes of Age

BY ROBERT SIDNEY DICKENS, DICKENS, INCORPORATED

In very recent years so much attention has been focused on the subject of package design that the *real* status of a package designer has begun to take on an *unreal* quality. Because fancy is always more exciting than facts, there have been many myths built up about package designers, few of which are really justified. Some of these myths have been started by package designers who talk too much but not too wisely. Sudden demands for services of a very limited profession in the past has been very heady brew for some designers.

By and large, the design profession has now settled down into a group of serious, knowledgeable and competent performers. Such groups as the Package Designers Council, for example, are doing an excellent job of exchanging information, setting up standards of performance and policing them, and creating a code of ethics which should eventually appeal to the most astute and hard-bitten business man with which designers deal. But this takes time and the myths still persist. The profession is still so new as such that it has had neither the time nor money to do a first-rate public relations job to dispel these myths.

I wish to explain briefly what a package designer is, what he can do for you, what he *cannot* do for you, and what his probable role in the future will be. But first, I must define a professional package designer, to start out on the right foot.

A professional package designer is an individual with a graphic arts background who has specialized and trained himself so that he can offer broad knowledge and experience in the field of *total* presentation of the packaged product. He may operate alone or head up a group of designers. He must, however, be able to offer unbiased professional advice and counsel in all phases of packaging. Whether he does all phases of the work himself, he must be able to provide these services and judge them. For example, only a few of the package designers are really packaging engineers, but they have the know-how to work with packaging engineers to get a result for their client.

A professional package designer must be able to start with the client's problems, know how to discover these problems if the client is unsure of his own direction, know how to see that the package is appropriate for the product, understand how to build in the right shelf appeal for the right product, be able to produce the most reproducible form of artwork and police the printing and production until the product finally appears on the shelf. While his services may have stemmed from an art studio in the beginning, a professional package designer is not just another commercial artist with a service to sell.

There are three basic types of designers in the package field. First, the so-called captive designer who works for a supplier of packaging products. Second, the package design director who works on a payroll of a company producing packaged products. Third, the independent professional package designer who operates his own organization and works directly with the manufacturer on a design fee or retainer fee basis. You will find equal talent and ability in all three types. As in all fields, you will find some extremely capable people and some mediocre talent. Because I represent the independent package designers, my discussion is confined to his role in merchandising today.

While our methods may vary somewhat, all package designers have one definite goal in mind. That is, to move more merchandise off of the shelf. To provide background and insurance for his judgment, the package designer must operate somewhat like a doctor. He must have all of the facts before him before he can write a successful prescription. He must talk with the manufacturer to determine as much about the product as he can, and to learn what his competition will be in the field. He must talk to the advertising agency to learn what their plans are for the advertising and promotion of the product. He must go out into the supermarket or wherever the product will be sold and bring back his own type of visual evidence of the product under its actual selling conditions. He must know whether it will be seen at eye level, above or below eye level, in the refrigerator case, or just before the customer reaches the check-out counter. He must see it against all of its immediate competition. He must even study all of the perimeter competition—in other words, he must know, not only what the package will compete with in its own field, but also what will compete for the attention of the customer in the surrounding area.

Only after he has all of this information and has studied it carefully, somewhat as a doctor would

(*Continued on page 109*)

*Presented at the 20th annual National Packaging Forum of the Packaging Institute, Inc., in Chicago, Ill.

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UCON Propellant 113 Trichlorotrifluoroethane
UCON Propellant 114 Dichlorotetrafluoroethane

AEROSOLS BOOST OVER-ALL SALES

BY ARTHUR KREINIK DANA PERFUME CORPORATION

By introducing a substantial number of new customers to the use of fragrances, aerosol packaging has brought the industry important new volume. Spray packages have certainly brought the Dana Perfumes Corporation "plus" business that has contributed greatly to the firm's progress and profits in the past few years.

A substantial amount of our aerosol volume has been new business—and not at the expense of our conventional packages. We can be sure that aerosol packaging creates new customers, because the sales figures for our colognes in conventional glass containers have increased impressively, too, over the past four years.

Aerosol packaging has really helped the entire fragrance industry, because it has popularized the use of scents. The ease of application and the non-spilling convenience of aerosols are highly effective sales features that have appealed to women who hadn't used fragrance before.

Aerosols are a permanent part of the fragrance business, not just a passing packaging fad. Far from being a gimmick, aerosol packaging has a basic appeal and utility that assures aerosol colognes of a continuing share of the fragrance market. The proportion of aerosol sales to conventional package sales is now relatively stabilized, I believe, and we can expect aerosols to continue to grow as the entire industry progresses.

Dana introduced its first aerosol in 1953. In the tradition of fragrance manufacturers, the company was seeking a unique and promotable idea to keep the firm in the forefront of the industry. There were already some aerosol fragrances on the market, but they hadn't achieved wide popularity.

The aerosol concept was not entirely new to us at that time. As early as 1951 we had toyed briefly with the notion of packaging our colognes in an aerosol can, but we decided that a container can was incompatible with the very nature of fragrance.

Then, plastic-coated glass bottles were perfected by the Wheaton Plastics Company, and special glass bottle valves were developed by The Risdon Manufacturing Company.

So, we returned to the aerosol concept.

Until then, aerosol fragrances had been packaged in stock bottles. Dana officials were convinced their package should have greater eye appeal, to be compatible with a woman's dressing table. Consequently, Javier Serra, our president, designed a shapely, tapered, plastic-coated glass bottle for the first aerosol cologne packages, and it has now become standard for all our aerosol colognes. The same package has been adopted, too, by Dana's French affiliate, which originally sold an aerosol fragrance in a can package.

Of the six fragrances then in its line, Dana introduced five as aerosols: Tabu, 20 Carats, Ambush, Emir and Platine.

Each of the five was packaged in a bottle of its

(*Continued on page 112*)

Appearance . . . performance . . . economy . . . these are the factors to consider when ordering cosmetic containers. On all three counts, you can count on *Calumet* to give you the most for your packaging dollar.

Calumet containers, whether designed for liquids, creams or solids, have a fine-quality look that consistently pays off at the point-of-sale. Precision-engineered for simple, foolproof operation, they perform easily and dependably. Mass-produced under the latest methods, they are spectacularly low in cost for their high quality . . . enabling you to realize substantial unit savings with subsequent profits. (Calumet containers are easily filled, too . . . a further economy in your manufacturing costs.)

Although *Calumet's* extensive line covers most current toiletry preparations, our superior research and development facilities, *plus* our long experience in the field, are always at your command in the solution of any special or unique container problem.

We shall be happy to supply samples, quotations and full information on request. Call OXford 7-6750 or write or wire to:

CALUMET MFG. CO.

565 Fifth Avenue, New York 17, New York

Canadian Affiliate: Eric H. Hardman Limited, P.O. Box 503, 1 Prince Charles Road, Brantford, Ontario, Canada

SPECIFICATIONS:

1. **ROLL-ON APPLICATOR**
   Features: Large ⅞" Ball in self-sealing container. Provides greater coverage with minimum time for application.
   Use: For hand and face lotions and liquid deodorants.
   Colors: Solid color or combination of colors.
   Capacity: 1½ oz. (app.)

2. **Oval SOLID STICK APPLICATOR***
   Features: Propel-Repel. "He-man" size. Convenient oval shape for maximum surface coverage.
   Use: For pre-shave, after-shave, and solid deodorants.
   Colors: Solid color or combination of colors.
   Capacity: 3 oz. (app.)

3. **CREAM APPLICATOR***
   Features: Propel-Repel. Applies directly to area, in quantity desired. Rub-in and massage, eliminating application with fingers.
   Use: Beauty creams, deodorant creams, unquents and medicated creams.
   Colors Solid color or combination of colors.
   Capacity: 1½ oz. (app.)

4. **Standard Round SOLID STICK APPLICATOR***
   Features: Propel-Repel. Airtight container.
   Use: Colognes, deodorants, and medication stick.
   Colors: Solid color or combination of colors.
   Capacity: 1½ oz. (app.)

Swivelpak® stick containers also available in ½ oz. and 1 oz. sizes.

*REG U.S. PAT OFF.

Packaging and Selling

What do you expect your advertising to accomplish? This seems like a very elementary question and the answer, with a snort of impatience, should be, to sell more goods.

Actually, modern business expects advertising to accomplish a great many different things. Of course, it is basic that in order to pay the advertising bill advertising must increase sales, but there are other very important secondary results which many businesses, in fact, most businesses expect to have happen as a result of the dollars they spend in advertising.

Just recently an article in Dun's Review And Modern Industry cited some of the basic things that advertising should accomplish and, as a very valuable corollary, some of the things that it should not be expected to accomplish.

These findings should be useful, not only to clarify any business man's thinking about the direction his own advertising should take, but to facilitate a closer appraisal of what he as an individual businessman is getting out of his advertising.

The first basic and obvious thing that advertising should accomplish, according to this business magazine, is the building of "a brand name that will create consumer acceptance, perhaps even consumer demand."

This is undoubtedly the primary objective of all advertising, but it is also the aspect about which there is more misunderstanding, more misinformation and more garbled thinking than there is regarding any of the other things advertising is suppose to accomplish.

Such current words as consumer demand, consumer acceptance, consumer recognition, consumer franchise and a hoard of others attempt to define just what advertising can hopefully accomplish in the mind of a consumer or a cross-section or group of consumers.

Some years ago a leading advertising agency came up with an analysis in which they said that no advertising appropriation of less than $250,000 a year could hope to gain even consumer recognition. This was followed by a great deal of discussion pointing out that this minimum had risen to $500,000. In the present period of enormous deluge of competitive advertising from television, radio, magazines, newspapers, car cards, outdoor signs and other media, it is exceedingly doubtful whether anything less than a million dollars a year in this enormous country of 175,000,000 people can gain a degree of consumer attention that will have a worthwhile, direct influence on retail sales.

This means that those people spending from two or three hundred thousand dollars a year up to a million dollars a year are rarely able to be heard in the ceaseless clamor of advertising; they can hardly expect to achieve anything like a consumer demand or a consumer franchise. They are, in fact, struggling merely to gain that still desirable but secondary result, namely, consumer recognition, the field in which advertising largely falls flat on its face unless the advertiser has secured a parallel degree of active store cooperation at the point of sale.

Anything under $250,000 should be generally classified as advertising used to bluff the retailer into some degree of retail cooperation, to lend its own sales effort to the merchandise.

For this reason, we seriously qualify an advertising appropriation if we say that its primary objective is to build a brand name that will create consumer acceptance or consumer demand. The one big question is, "How much are you spending?"

The second desirable result that can come from advertising, according to Dun's Review is the introduction of "new products, new improvements, and new ideas almost overnight to the public."

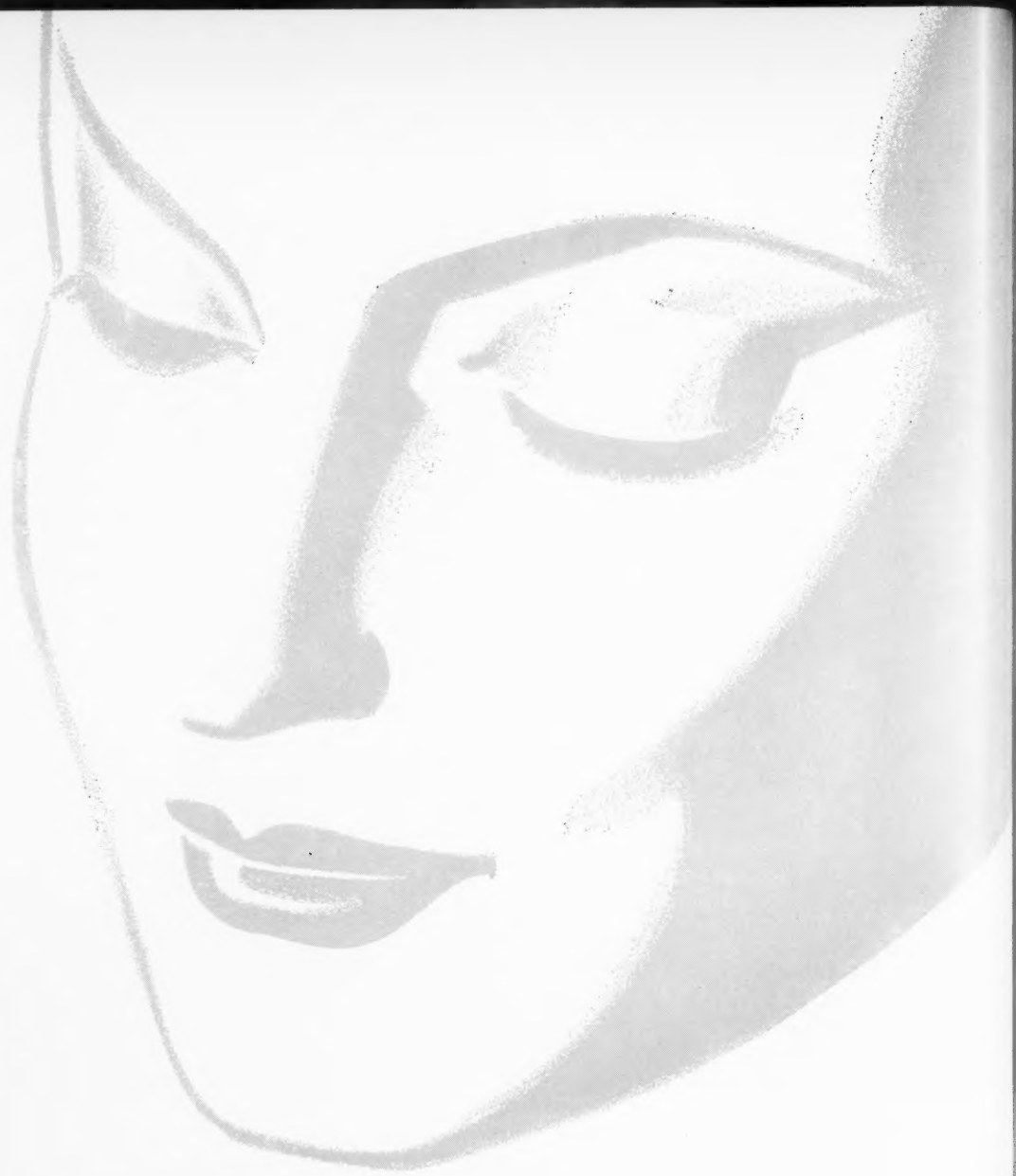
The phrase, "almost overnight," is surely a catch. Take the case of one of the big "Soapers" said to have spent $18,000,000 in three months to introduce a new product; or the case of another whose president reported to stockholders that a product would not even be considered unless it justified an expenditure of $5,000,000 for its introduction.

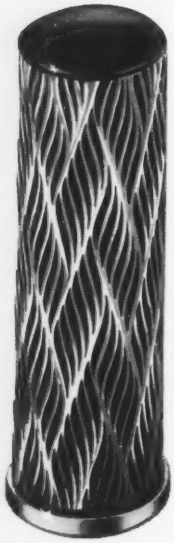
Advertising can and does introduce new products. When millions are employed, it can conceivably be done overnight, but when you pare expenditures to a million or a few hundred thousand dollars you have a hard, upward pull.

As a matter of fact, if you are not in the multi-million dollar class, you can do a much better job of introducing a new product by getting the cooperation of the big retailers who combine a heavy daily traffic with creative sales ability and a high degree of favor among the people in their community.

The third favorable result that can be obtained by advertising is to "create an image of your company valuable in attracting good personnel and investment capital as well as creating good public relations for your company."

Many big companies expect this indirect result from their advertising. It is always an extra dividend from good advertising, but one should remark that it is something normally obtained by a type of advertising such as institutional advertising, which is not





WIN HER WITH THE LOOK OF ELEGANCE

Lambert ENGRAVING

ADDS TO YOUR PRODUCT

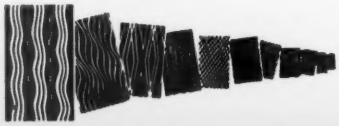
Just as there is nothing quite like elegance to enhance your product's sales-appeal . . . there's no substitute for engraving and engine turning to achieve the *look* of elegance.

A refined gracefulness is *not* synonymous, however, with high cost — when you turn to Lambert for engine turning. Here in Attleboro, we have coupled the art of single tool craftsmanship with Lambert's exclusive *multitool* process, to give you *quality in quantity.*

Quality-in-Quantity engine turning
makes elegance practical

If you would like us to ornament a sample — to demonstrate how Lambert design talent and engine turning can make your product elegant in all but cost — please write enclosing several shells. There is no cost or obligation.

Lambert Engraving Company, Inc.
Attleboro, Massachusetts



specifically directed to increasing sales. Moreover, it is normally a long-range result of advertising and rarely the result of a high-pressure competitive campaign. Such objectives as obtaining investment status often mean an advertising investment in a type of media, for instance, in certain magazines, that bears little or no relation to the consumer market for that company's product.

In other words, although this objective often comes about from good product advertising, it is usually achieved most effectively as the outcome of a campaign planned specifically for this purpose.

Another goal of advertising is to "obtain distribution for new products and widen distribution for older items."

Considerable consumer advertising used to be sold with the hope of thereby getting distribution, and this is still done to some extent. Actually, experience shows almost universally that this is a colossal waste. Unless the advertising campaign is a multi-million-dollar high-pressure onslaught, one of the surest ways of wasting money in business is by trying to buy distribution through the use of consumer advertising. The results of advertising are slow to accumulate, and by the time anything approaching the kind of demand that will arouse the dealer happens, a good many thousands of dollars can go down the drain in territories where the distribution is inadequate.

Distribution is economically secured by salesmanship plus good trade relations plus a lot of other promotional activity and advertising to the trade. When consumer advertising is properly geared to this well-thought-out strategy, it is a possible adjunct in spreading distribution.

As to what advertising should not be expected to do, there are, of course, many admonitions.

For instance, according to Dun's Review, it should not "be expected to do a precise job and produce a precise result—at least, at this stage of its development," which seems about as elementary as any rule could be and requires no further comment.

Secondly, advertising should not be expected to "produce miracles—it cannot enable you to buck a basic consumer trend." Just about the hardest thing in advertising would be to sell that idea to a lot of hopeful Harrys and a lot of big spenders. As a matter of fact, if advertising ever could be reduced to an analytical case study, we should find that a lot of big national advertisers and big advertising agencies have been plunging with a lot of money for no more basic reason than their hope of a miracle.

Advertisers are also admonished not to try to "put over an inferior product by sheer quantity or quality of words, no matter how much money you spend." This ought to be an axiom, yet nothing could be further from the everyday practice of advertising. The cosmetic industry in particular, swamps the market each year with casual, half-baked products and imitations on which they hopefully invest quite a bit of advertising money. It is probable that a conservative one-third of all advertising expenditures would evaporate if this rule were rigidly applied by every business.

Advertising, in the fourth place, cannot be expected to "work effectively if management makes the advertising budget a catch-all for every expense it can't charge elsewhere." This admonition is really a great big laugh—you would have as hard a time as Diogenes with his lantern to find a single company that does not load all sorts of extraneous gimmicks, evasions and bookkeeping gymnastics on the advertising budget. Advertising and promotion is one section where the tax man is usually not too critical. It just would not be fair to ask anyone to get the advertising budget too pure.

Finally, advertising cannot be expected to "function efficiently if used for vanity purposes." If this were applied universally, it would kill a certain amount of advertising and take a lot of fun out of other advertising. It would be very tough on television, tough on certain prestige business magazines and, in fact, for some men, it would take all the pep and fun out of their club membership.

Just think how many businessmen have been given a proud and happy day with wonderful news to tell the wife when some big industrialist at the Union League Club has casually remarked to him, "I saw your ad in Fortune."

That is, if it ever happens!

Herbert F. Storfer, executive vice-president of Parfums Corday, Inc., summed up what manufacturers are up against in cooperative advertising at the recent fragrance convention this way:

"How about advertising? Is cooperative advertising really cooperative—when the store emasculates the basic copy theme? Or when inflated rates are quoted to the salesman?

"Can an ad work effectively when the advertised merchandise is not displayed prominently in the department, or must we depend strictly on mail order or 'total recall' on the part of the consumer?

"Here's one with which I have had recent experience. . . . How many fashion coordinators, when they give samples of a perfume in their shows, ignore the A.B.C.'s and forget to ask the women to open her gift and try it on?

"How many stores have closed one of the most productive of all forms of promotion to us—perfumed inserts—because one person in 50,000 complained?"

Deodorant sales continue to plow ahead as one of the few dynamic products of the cosmetic industry. In addition, this product seems to have one of the most favorable margins for expansion in the entire industry.

Small wonder then, that everybody is joining the deodorant parade with new products, new packaging, new methods of dispensing and greatly expanded advertising appropriations.

There seems to be a new exuberant expansion in the men's field for the deodorant. This is because unquestionably there has been a substantial growth in sales of the deodorant brands specifically confining their appeal to the masculine market. Just why there should be separate deodorants for men and women escapes us for the moment.

We suspect that this separation is a temporary phase in the development of this important cosmetic, which is taking place only because most men using deodorants are new converts, a very high percentage of males are still to be convinced.

It does seem to us, however, that the deodorant field is waiting for a brand with a sufficiently compelling and striking advertising campaign to wash out this difference in sex preference.

Undoubtedly, the new ownership of Seaforth, Chesebrough-Pond's, will give a new mass-market impetus for the Seaforth deodorant, probably by a greatly enlarged advertising program.

As a matter of fact, it is very likely that the new deodorant brands for men will marshal more weight in advertising and in selling than those for women. When you combine Mennen, Shulton, Warner Lamberts Sportsman, Chesebrough-Pond's new Seaforth line, together with Helene Curtis' Kingsmen and, probably, Bristol-Myers new men's roll-on, Trigg, you discover a competitive accumulation with a great deal of weight.

The deodorant business has three big fields of expansion. One is the very large section of men not now using any deodorant—probably between 40 and 50 per cent of all men. The second is among the large proportion of current deodorant users, both men and women, to increase the frequency of use. Finally, it seems to us that there is a big opportunity to level out the seasonal variation in deodorant sales and use. Certainly, as things stand now, advertising, selling and all promotional effort is concentrated during too few months in the year.

Here's the best way to determine the size of your advertising budget, according to a recent quote: "We don't dare spend less and we can't justify more."

The really hot question of this year may be: Are some of the policies of the big national manufacturers driving the retailer pell-mell into private label?

It seems as if a very strong movement in this direction is already on the way among the big food chains.

Just recently a top food executive let off a full-fledged blast at "unrealistic pricing" of some national brands. This executive noted that store-label margarine is selling for 8 cents per pound less than branded labels; a 3-pound can of shortening is 19 cents less than national brands; a quart of private-brand mayonnaise is 10 cents less than national labels; a giant package of detergent is 14 cents less than national brands.

According to this executive, "In every instance, the private label gives the merchant more profit. It is ironic that the private labels are made by national-brand manufacturers."

There is nothing new about the private label among the big food chains. What is new is the increasing percentage of store sales which these labels are taking, and the increasing number of food executives who are talking more and more about private label.

As just one instance of the growth of private brands, it was recently cited that a leading national chain operating in California sold $50 million worth of its own frozen brands as against a total sale of $80 million in frozen foods.

In this industry the private label has never recovered from the almost mortal blow dealt to it during the war, when many stores—particularly drug chains and department stores—well intrenched in private label, were forced to discontinue their store brands because they could not compete with manufacturers in the hectic rush for alcohol, packaging materials, many chemical raw materials and other things needed in their manufacturing operations. By the end of World War II, about 80 per cent of the well-known retail private labels in this trade seems to have been wiped out.

There have been other reasons why the large majority of retailers have been reluctant to enter into manufacturing. One reason is that hardly any retailer ever seems able to think in terms of manufacturing. As a matter of fact, since retailing is a full-time operation taking all the resources in time, money and creative thinking, the private-label manufacturing division usually ends up in the control of some minor-salaried individual who would be exactly that if he were employed by a manufacturer.

Another reason is that the retailer is not in any way exposed to the flow of invention and creative thinking that takes place in the supply trade among the package manufacturers, the chemical and the raw material manufacturers, equipment manufacturers and others. This constant flow of inventiveness and creative thinking in the supply trades is probably the most essential advantage that a manufacturer has, as against the private label of the retailer.

This is doubtless why, in almost every case, the retailer's private label operates simply as an imitation of the popular and acceptable national brands.

In spite of all the disadvantages the retailer discovers in his private-label operation, he is increasingly finding advantages that balance the scale, and in some cases tip it in favor of the retailer's brand.

One of these is that a great many manufacturers

1875

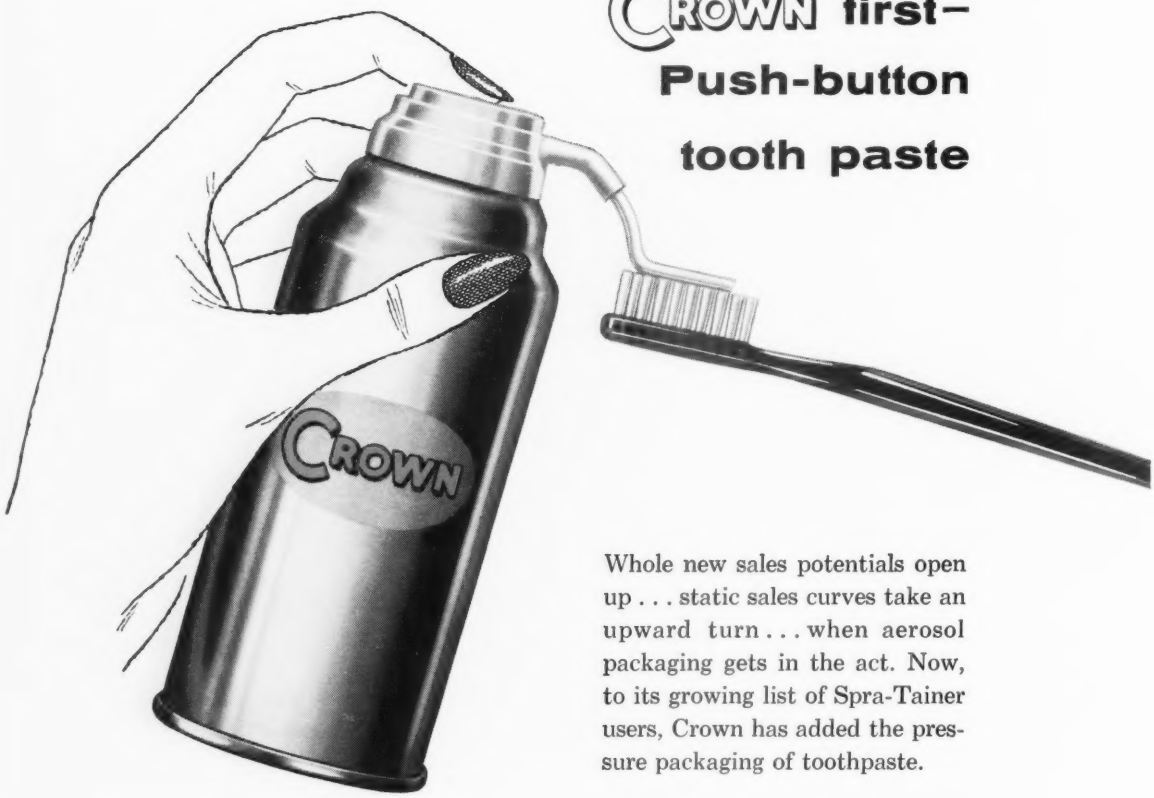
. . . Back in the cracker barrel era, dapper derbied salesmen began to show their products packaged in glass containers. The public liked what they "saw," and glass factories began to flourish. Today Metro's modern glass containers, reduced in weight, sanitary, odorless and available in clean, eye-catching designs, help sell many of the best products made. Metro research does away with guessing . . . Metro speed meets your time schedule . . . Metro quality can't be beat. That's ***metromatic . . . when you need it!***

MANUFACTURERS OF QUALITY GLASS CONTAINERS

METRO GLASS

METRO GLASS COMPANY, INC., GENERAL OFFICES: JERSEY CITY, NEW JERSEY

Another CROWN first– Push-button tooth paste



Whole new sales potentials open up . . . static sales curves take an upward turn . . . when aerosol packaging gets in the act. Now, to its growing list of Spra-Tainer users, Crown has added the pressure packaging of toothpaste.

Crown, who pioneered the aerosol can with Spra-Tainers, has continued to expand production facilities in the aerosol field . . . offers the most complete line of aerosol cans available in both the seamless and fabricated styles.

If you want to capitalize on the profit potential of the push-button age, call the man from Crown and consult with him on methods of aerosol packaging. Crown Cork & Seal Company, Inc., Can Division, 9300 Ashton Road, Philadelphia 36, Pa.

for closures
for containers
for machinery

CROWN

CROWN CORK & SEAL COMPANY, INC.

have been stretching too far the distance between the finished cost of his product and the list price, which he determines the consumer must pay under fair trade. This differential has been so expanded, to take care of the constantly growing advertising expense, that retailers now find a very juicy difference between the cost at which they can obtain the product unbranded and the list price of the branded product.

Another factor that seems to be operating is the competitive expansion into more and more national advertising, which has encouraged many manufacturers to venture into increasingly broader distribution. This ever broadening distribution has resulted in a retail dilution for many brands, which means that sales per store do not provide significant competition against the retailer's own label.

Before World War I we had a modestly favorable climate for the retail private label in which only a limited number of very large retail units could effectively establish a worthwhile position. During the war most of these brands were wiped out but in the succeeding years, conditions have slowly reverted. until there is now a definite balance of favorable and unfavorable factors.

In the food field, at least, the trend seems definitely in favor of growing private label. It remains to be seen whether a similar trend will develop for the products of this trade.

According to reports in the grocery store press, vitamins are apparently becoming particularly attractive in the health and beauty department of supermarkets. As an officer of one of the major coastal chains recently reported, vitamins open an opportunity for the supermarket for a new conception in merchandising.

According to this executive, "We should sell vitamins in markets as food supplements, rather than as a doctor's recommendation." This market has already moved aggressively to achieve its objective with newspaper advertising and special point-of-sale display.

We do not know who first used the phonograph record to get the physician's attention, but we remember several years ago that Elmer Bobst initiated a mailing campaign to physicians using a series of records with classical music on one side and a dissertation on Warner products on the other.

We never heard just how this clicked, but we were under the impression that it did not go over too well because it was not a continual program.

Now the pharmaceutical division of the Borden Company has decided to use long-playing records in a series called "clinical conversation pieces." One subject is cosmetic sensitivity and another is the allergic history.

According to Variety Store Merchandiser, the drug and cosmetic department has shown an increase in variety stores for the first time in many years.

The three main reasons are the expansion of proprietary medicines, of men's toiletries and of beauty preparations for women. Men's toiletries are finding more and more space on variety counters, according to this authoritative publication.

A new survey by Redbook shows some interesting variations among age groups in regard to cosmetic and toiletry shopping habits. Younger women show a decided preference for suburban shopping centers.

The 1958 Beauty Reader Forum of the Fawcett Publications is now available.

Conclusions: Continuing popularity of the "natural look;" most women still own three or more lipsticks, with true red the most popular shade; light pink is the first choice in nail enamel; a slight increase in the use of preparations designed for particular skin conditions and skin types.

As one victim of one of the biggest bust-ups in advertising history, 'The $64,000 Question" has finally been cancelled.

This famous quiz show originally sponsored by Revlon, which introduced that wonderful era of the magnificent give-away, closed its books with a history of handing out $2,106,800 in cash as well as 29 Cadillacs.

Fragrance is an essential, perhaps the essential factor, in bath preparations. This is a conclusion in a survey recently made for the Toiletry and Cosmetics Division of Owens-Illinois Glass Company.

Pine fragrance is most frequently purchased by users of bath oil, while apple blossom is second and carnation a poor third. The leading fragrance in bath salts is apple blossom, with pine and carnation in second and third places. Apple blossom is also the preferred fragrance in bubble bath. Pine and carnation are second and third.

Below is a study of the sales of drug and cosmetic classifications in a leading supermarket, Food Fair, for the six-month period from January 1 to June 30, 1958. This detailed study was reported as part of a classification of sales in every department of this supermarket in the September issue of the magazine Super Market Merchandising.

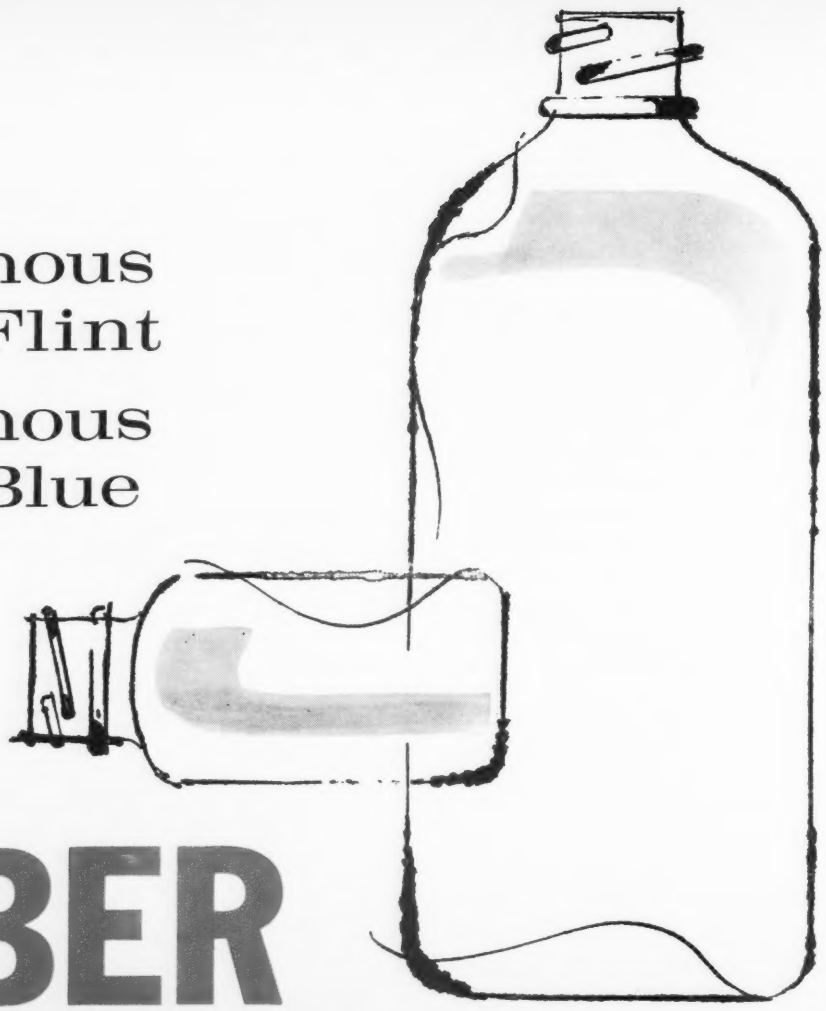
During this six-month period, the total sales of this chain was $35,301,000.

HEALTH AND BEAUTY AIDS

	No. of Items	No. of Brands	Weekly Dollar Sales	Weekly Dollar Sales Per Store	% of Product Classification
Health & beauty aids	284		$32,886	$1,217.98	100.0%
Drugs	67	27	7,892	292.30	24.0
Hair needs	79	37	9,781	362.25	29.7
Dental needs	34	17	6,646	246.15	20.2
Cosmetics	56	34	4,236	156.89	12.9
Baby needs	23	9	2,474	91.62	7.5
Shave needs	25	15	1,857	68.77	5.7

Famous
for Flint

Famous
for Blue



NOW

AMBER MARYLAND GLASS

Designing, creating and manufacturing glass packages that sell is nothing new for Maryland Glass. We've done it successfully for years. Famous Maryland Blue bottles and jars have stopped the eye . . . and started the sale for dozens of products; the quality designs and distinctive shapes that Maryland has created in crystal clear Flint Glass have long been a byword with men who recognize that a well dressed package is the best introduction for a quality product.

Now there is something NEW at Maryland Glass. The same imagination in design, the same service and experience are available to you in eye stopping AMBER GLASS.

If you have a design problem or a packaging need . . . IN BLUE, FLINT, OR AMBER get in touch with MARYLAND GLASS CORP., 2147-53 Wicomico St., Baltimore 30, Md.

News in Packaging . . .

Canco's New Pricing Policies To Result in Savings on Cans

The American Can Company recently announced basic and far-reaching changes in its metal can pricing that will mean lower can prices for most of its customers. "These changes, with substantial economies we have achieved through our coil processing program, will mean an aggregate saving to our can-using customers of over $9 million," according to William C. Stolk, president.

The change is the elimination of the method of averaging can prices over broad geographic areas. Instead, Canco is establishing a separate f.o.b. price at each of its plants for each type and style of can. This policy means that the firm's prices "now will reflect to customers the freight-cost advantages of their nearness to the steel mills," he said.

Self-Sealing Corrugated Boxes

Corrugated boxes that can be assembled and sealed by merely pressing precoated flaps together are available from Stone Container Corporation. When matching strips of the coating, called Stik-Kwik, make contact, a strong cohesive bond is formed. The bond has high shear and tensile strengths, but seal can be opened with the hands, since the coating sticks only to itself and not to untreated box areas, hands, clothing or other surfaces.

Light Polyethylene Bottles Offered by Continental Can

New linear polyethylene bottles that are lighter than regular polyethylene bottles by as much as 40 per cent and resistant to high temperatures are now available from the Plastic Container Division of Continental Can Company. The Conolene bottles are available in many sizes and shapes, including a Modified Cylinder Design in 12- and 16-ounce sizes, which are easy to fill.

The gas permeability in linear polyethylene is 1/3 to 1/4 less than that of conventional polyethylene and liquid permeability is 1/3 to 1/6. Stronger and tougher than conventional polyethylene containers, these bottles are non-toxic, and they are suitable for packaging products at higher temperatures without collapse or distortion.

Anti-Adhesive Silicone Coatings

Syl-off silicone paper coatings that supplant kraft, glassine, parchment, multiwall bag liners, boxboard, plastic film and other packaging materials are being manufactured by T. M. Dow Corning Corporation. These coatings are said to be comparable and, in some applications, more economical than other surface treatments, and to impart excellent release characteristics, to be water repellent and permanent. Moreover, they will not contaminate, migrate or alter stocks or packaged products.

Furacin Solution Veterinary, used in treatment of bovine mastitis and intra-uterine infections, in a single-dose, squeeze dispenser. The accordian-like polyethylene syringe was developed by C. Weckesser, Norwich Pharmacal Co. for Eaton Laboratories, a division.

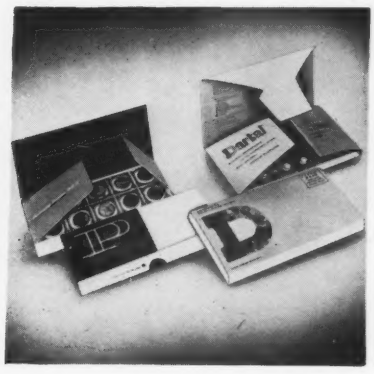
Polypropylene High-Temperature Plastic Has Unlimited Uses

Dr. J. A. Neumann, president and director of research, American Agile Corporation, recently said that the future of the newly developed polypropylene high-temperature plastic shows unlimited possibilities for varied uses in industry.

The most outstanding property of polypropylene, Dr. Neuman pointed out, is its exceptional resistance to heat. Its melting point is more than 300 degrees F., and the plastic has a Vicat softening point greater than 185 degrees. These characteristics make it possible for parts manufactured from polypropylene to be sterilized in boiling water or steam, since the material behaves as a crystalline solid even at temperatures above 212 degrees. Moreover, the plastic's molecular structure gives it far better chemical and stress crack resistance than most weldable plastics.

Winners of the 1958 Packaging Design Awards for push-button aerosol products presented by the Aerosol Division of the Chemical Specialties Manufacturers Association (left to right): Gillette Foamy Shaving Cream, Gillette Safety Razor Co.—category of shave products; Brite Set Hair Spray, Cara Nome—hair preparations; Chanel No. 5 Spray Cologne, Chanel, Inc.—perfumes, colognes and toilet waters; D.C.S. Cutting Oil, A. W. Chesterton Co.—industrial products; Nail Dri, A-M-R Chemical Co.—other personal products; Quik Spray, Sheffield Bronze Paint Corp.—paints, etc.; Sizzl-SP barbecue sauce, Andersen Foods—food products; Insect Killer, Electrolux Corp.—insecticides, repellents and moth proofers; Fungi-Rex Athlete's Foot Spray, Rexall Drug Co.—medicinal and pharmacutical products; Klean-Air, Avon Products Corp.—room deodorants; Sprayrite Animal Repellent, Virginia Smelting Co.—other household products.

New cushioned self-mailer which enables mailings in small quantities of individual drugs and pharmaceuticals, by Ivers-Lee Co. Units can be sealed in a variety of heat-sealing materials in this Super-Sealtite Unit-Package.



another RICHFORD First:

TOUCH-N-SPRAY

TRADEMARK

THE ALL PURPOSE AEROSOL PERFUME ATOMIZER FOR THE PURSE

TOUCH-N-SPRAY Refillable ...

TOUCH-N-SPRAY Long Gold Metal cap to prevent accidental activation.

TOUCH-N-SPRAY So easy to use—so light in weight—so very, very smart.

Write NOW for samples and prices

RICHFORD CORPORATION

Offices & Plant
3618 Oceanside Road
Oceanside, New York

Salesrooms
350 Fifth Avenue
New York, N. Y.

ADVERTISING NOTES

BY TED KLEIN, PUBLIC RELATIONS DIRECTOR*

Health Professions

A recently published report from the Census Bureau details the growth of certain professions from 1920 to 1950. The number of physicians has increased a mere 35 per cent during the 20-year period. In marked contrast are the engineers who have increased 300 per cent, accountants 200 per cent and optometrists 100 per cent. In 1920 there were 64,236 pharmacists; in 1950 there were 90,307. The veterinarians have stayed at about the same level during this period with 13,494 in 1920, and 13,679 in 1950. For many years the physician-to-population ratio in this country has been about 130 to 100,000 or 1:770. In the past ten years the number of physicians has increased from 197,605 to 226,625. However, many recent graduates are not engaged in caring for patients, having chosen research instead of active practice.

The problem of meeting the needs of increased population is always the subject of the medical educator's speculation. Last year, for example, the American Medical Association reported that 619 budgeted, full-time medical school faculty positions were unfilled. This was an increase of over 90 per cent from the previous year. Obviously, we can't train more physicians unless we have the teachers and the teaching facilities. Today, many would-be physicians are taking graduate degrees in the physical and biological sciences, rather than seeking MD's as they would have a few years ago. Medical educators in the future may well be forced to find means for encouraging more teaching physicians. Or, is it a problem not so much of increasing the number of physicians, but rather of finding improved and time-saving methods for the diagnosis and treatment of patients?

To Tell the Truth

Top McKesson & Robbins executives are taking to speakers' platforms across the nation this winter to tell a story titled "What Price Your Life."

The speakers (the best in each of the eight McKesson Wholesale Divisions) will use a new color film strip to illustrate their talks, which will feature the facts of the drug business. Prices are given to prove that drugs are the best investment anyone can make when illness strikes. Average net profits of wholesalers, retailers and manufacturers over the years are given to document the statement that the public is getting more than its money's worth in prescriptions.

McKesson's Dudley Taw, head of the Drug Relations Dept., reports that Kiwanis, Lions and Rotarian organizations are eager to have the McKesson's film strip shown.

Here is one of the best recent examples of informed, constructive public relations we have seen. The film strip is beamed at the public. Its message is short and to the point: "You, the consumer, are getting the biggest bargain there is when it comes to drugs."

Wise Words

Merck's director of public relations, John Horan, believes that the industry had better take to the battlements immediately to fight the increasingly hostile press on drug prices. Speaking before the National Drug Trade Conference in New York, Horan said, "We have nothing to fear from an informed public, but unless we act promptly and effectively, we may see the seeds of our industry's destruction sown in public misinformation and misunderstanding."

We add our voice to that of Mr. Horan. We, too, cannot help but wonder when the industry will go into high gear on a mass public information campaign on drug prices. We suggest the time is now.

The Role of Public Relations

At the conference Roy Larsen, president of Time Inc., spoke on the part public relations plays in today's economy. "Professional public relations," he said, "has been the activating force in releasing for the public good the tremendous resources of manpower and wealth represented by the American corporation. Advertising could point out the accomplished fact, but it could not bring it about. Public relations could and did supply the motivation."

Churchill on Advertising

I think one of the best definitions of the role of advertising was given by Winston Churchill in a book put out by the *Reader's Digest*:

"Advertising nourishes the consuming power of men. It creates wants for a better standard of living. It sets up before a man the goal of a better home, better clothing, better food for himself and his family. It spurs individual exertion and greater production. It brings together in fertile union those things which otherwise would have never met."

Peck's Good Girl

Few fields are as individualistic as ours. The number of experts and professionals far exceeds those who toil in the plants. But there is even more professionalism in the world of the high fashion magazines. There, the masters are few, the masses many.

The leading youth fashion book, according to many, is *Mademoiselle*. The leading writer of health and beauty features is Bernice Peck. Recently the magazine staff was joined by denizens of the world of cosmetics, advertising and publishing to pay tribute to "Peckie" at a party in Manhattan. The occasion was her retirement from the magazine she helped establish some 24 years ago.

We join with her many friends and admirers in wishing her well, and are delighted to learn that she will continue as a feature writer with *Mademoiselle*.

Bernice Peck, who is retiring as health and beauty editor of Mademoiselle, to carry on as a feature writer with the same magazine.

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Patent thoughts and trends

BY THOMAS CIFELLI, JR., PATENT ATTORNEY*

Two Armour ACTH Patents Invalidated

Two ACTH (adrenocorticotrophin) patents owned by Armour and Co. were recently invalidated by a U. S. District Court in Chicago in a suit against Wilson and Co. The patents referred to are U. S. 2,669,536, issued to Armour on an invention of Dr. Bunding, and U. S. 2,669,537, issued on an invention of Dr. Thompson.

The Bunding invention deals with a method of purifying ACTH by adsorbing the ACTH on an adsorbent and then eluting the ACTH in more purified form.

The Thompson patent deals with ACTH-gelatin compositions with and without additional ingredients such as PVP or aluminum phosphate.

The Court, in its opinion, reviewed the prior art and the development of the inventions in great detail. A reading of the opinion in full, therefore, will be most rewarding to those interested in a comprehensive summary of the early development in the practical use of ACTH. While the opinion of the Court touches on a number of aspects which might be considered purely legalistic at first blush, it is believed that a reading of the opinion will be very helpful to those who have anything to do with the preparation and prosecution of patent applications, whether from the point of view of the drafting attorney or the inventor himself. The opinion touches on certain pitfalls that should be avoided in the building of a strong patent.

Because of the general lessons that can be learned from a reading of the opinion in full, and because of the particular interest the opinion will receive in the drug field, the findings of fact and conclusions of law are being set out in full, except for omissions of references to the record of the case and to legal citations.

Before setting out the opinion it is to be noted that the losing party, Armour and Co., has the right of appeal to a higher Federal Court. At this writing the author does not know whether such an appeal is being taken.

The Court's finding of facts and conclusions of law, modified as above, are as follows:

Findings of Fact—Thompson Patent

(1) Plaintiff owns the Thompson patent in suit, No. 2,669,537, which was issued on February 16, 1954 on a continuation-in-part application, filed December 27, 1952, which was partly based on an earlier application filed August 14, 1950.

I. *There is no invention in the Thompson patent.*

(2) The hormone ACTH was known long prior to the Thompson patent, but the medical profession was unaware of a use for ACTH until Dr. Hench of the Mayo Clinic published his Nobel prize-winning work in the spring of 1949 showing the usefulness of ACTH in the treatment of rheumatoid arthritis.

(3) Shortly thereafter, in June, 1949, Dr. Klein of the Wilson Laboratories discussed with Dr. Wolfson the use of gelatin with ACTH to prolong its activity and thereby increase its effectiveness.

(4) Long prior to the Thompson patent, gelatin was well known as a vehicle to increase the effectiveness of drugs, being used "as a vehicle for subcutaneous injections when slow absorption of a drug is desired." Gelatin was used as a retarding agent both with and without additional ingredients just as in the Thompson patent. Examples of the use of gelatin without additional ingredients were shown in the literature with respect to insulin, epinephrine amphetamine, pollen extracts, penicillin, heparin and tubocurarine. Examples of the use of gelatin along with other ingredients were shown in the literature with respect to epinephrine, heparin, tubocurarine, codeine and morphine, suprarenin (adenalin), degitalis, ephedrine, morphine, codeine, strychnine, strophanthin, belladonna, caffein, pituitrin, antuitrin, pitressin, pitochin and "substantially all water soluble drugs suitable for subcutaneous and intramuscular injection."

(5) The gelatin so used, both with and without other ingredients, was long known to cause between twofold and eightfold increase in effectiveness of the drugs.

(6) The action of gelatin with ACTH is satisfactorily explained solely on the basis of retardation of absorption. Dr. Thompson in a communication within the Armour organization stated:

"The effect of gelatin on ACTH action can be quite satisfactorily explained on the basis of absorption control alone."

(7) Gelatin acts in the same manner with ACTH as it was long known to act with other drugs. Dr. Cluxton, plaintiff's then director of medical research, stated in an internal memorandum:

"Gelatin is such a well-known substance that only the pertinent qualities of this vehicle as concerns ACTHAR will be briefly mentioned. It may be administered intramuscularly or subcutaneously. Among the outstanding physical properties of gelatin is its stability in extreme temperatures and its broad solvent properties. It is an excellent viscous colloid permitting prolonged action of ACTHAR as well as heparin and other pharmaceutical products."

(8) The Thompson patent describes and claims the use of ACTH with gelatin, with or without additional ingredients. Examples I-III of the patent describe compositions containing ACTH, gelatin and phenol; Example IV describes an ACTH preparation with aluminum phosphate and the well-known Pitkin's menstruum (gelatin, dextrose, and acetic acid); Examples V-VII describe ACTH-gelatin preparations which include procaine hydrochloride, chlorobutanol trisodium phosphate, aluminum phosphate and polyvinyl pyrrolidone (PVP).

(9) Claims 1 and 2 of the Thompson patent are directed to ACTH-gelatin compositions broadly, that

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is, with or without additional ingredients; claims 3-7 are directed to ACTH-gelatin compositions plus additional ingredients such as PVP or aluminum phosphate.

(10) Thus, the subject matter described and claimed in the Thompson patent is nothing more nor less than the use of the well-known vehicle, gelatin, with ACTH, the therapeutic usefulness of which had become known through Hench's work, but a short time before. Such use of a well-known vehicle did not constitute invention.

(11) This finding of no invention is in full accord with the testimony of witnesses for both the plaintiff and defendant. These witnesses, all men skilled in the art, agreed that the use of gelatin with ACTH was "common sense, simply because everybody knew about the possibility of using gelatin as a long-acting agent" (Wolfson, Fersham, Frawley, Fisher and Hier). Dr. Leake, defendant's expert, who has spent his distinguished career working with pharmaceutical products and the only witness who was not cross-examined, testified to the same effect.

(12) It was not inventive to do the obvious, that is, use common sense, and the Thompson patent represents nothing more than this.

II. *Thompson was not an original and first inventor.*

(13) As a result of the discussion between Klein and Wolfson in June of 1949 (see Finding 3), Dr. Wolfson requested non-antigenic gelatin from Dr. Klein by a letter dated July 26, 1949 and Dr. Klein shipped such gelatin to Dr. Wolfson on September 12, 1949.

(14) The first clinical use of gelatin with ACTH was made by Dr. Wolfson on his patent Loidl on September 27, 1949.

(15) About October 1, 1949, Dr. Thompson was informed of Dr. Wolfson's work with long-acting ACTH and started cooperative work with him.

(16) On October 20, 1949, Dr. Thompson's notebook reveals that "Dr. Wolfson suggested combining all the known effective delaying agents, trying the combination clinically and, by elimination, trying to arrive at an effective preparation."

(17) Dr. Thompson's first written entry suggesting the possible use of gelatin with ACTH appears in his notebook on November 22, 1949. This was after several discussions with Dr. Wolfson and after Dr. Wolfson's use of gelatin with ACTH on his patient, Loidl.

(18) The common sense concept of using gelatin with ACTH was known to Dr. Klein and Dr. Wolfson prior to any such concept by Dr. Thompson, and an ACTH-gelatin preparation was used by Dr. Wolfson on his patient Loidl prior to the preparation of any such composition by Dr. Thompson.

(19) Dr. Thompson was not an "original and first inventor" of gelatin with ACTH.

III. *The first commercially accepted product was developed by defendant.*

(20) In June, 1951, Dr. E. B. Astwood published a paper teaching the use of a method of purifying ACTH with oxycellulose. Prior to Dr. Astwood's publication, defendant had been working with Dr. Astwood and knew of the oxycellulose method of purification.

(21) On June 20, 1951, Wilson prepared an ACTH preparation containing gelatin, Astwood ACTH and 0.5 per cent phenol. This material was sent for clinical testing to Dr. Wolfson on October 1, 1951 and to Dr. Forsham on December 17, 1951.

(22) In the fall of 1951, Armour marketed an ACTH preparation containing crude ACTH, gelatin, trisodium phosphate and propylene glycol. This preparation (known as ACTHAR GEL) was unsatisfactory.

(23) On December 27, 1951, plaintiff was advised by Dr. Forsham that the Wilson gelatin-ACTH preparation was far superior to Armour's ACTHAR GEL.

(24) Immediately thereafter, early in January, 1952, Armour obtained from Dr. Wolfson samples of the Wilson ACTH-gelatin preparation.

(25) Commercial gelatin preparations of the type presently marketed, which contain Astwood ACTH, gelatin and phenol were prepared by Wilson prior to any preparation of such products by Armour, and were prepared by Armour only after Armour had received a sample of the Wilson product from Dr. Wolfson.

IV. *The Thompson patent is barred by the statute.*

(26) The original Thompson application filed on August 14, 1950 contained no example of the use of gelatin and ACTH without either aluminum phosphate or PVP. Not until December, 1952, when Dr. Thompson filed his continuation-in-part application did any patent application of Dr. Thompson contain examples of ACTH, gelatin and phenol without other ingredients, and by that time, the Wilson product was already on the market.

(27) Armour marketed an ACTH-gelatin composition in the fall of 1951 (Finding 22) more than a year prior to the date of filing of the Thompson continuation-in-part application of December 27, 1952. This was "public use" more than one year prior to Thompson's effective filing date.

V. *Improper claim of inventorship.*

(28) In January, 1950, Dr. Wolfson suggested to Dr. Thompson that PVP be used with ACTH to retard the absorption of ACTH; Armour immediately cabled Europe to obtain PVP for experimental use.

(29) After Dr. Wolfson suggested the combination of ACTH and PVP to Dr. Thompson, plaintiff arranged to have Dr. Wolfson disclaim inventorship. Dr. Thompson thereafter claimed ACTH and PVP as his invention in his original application filed in August, 1950.

(30) Dr. Thompson continued his attempt to obtain a patent on ACTH and PVP until May, 1958.

(31) The use of PVP with ACTH was not the invention of Dr. Thompson. Plaintiff's action in seeking to patent it as a Thompson invention was wrongful.

VI. *Improper prosecution of the Thompson application-rat test.*

(32) Thompson's original patent application was rejected by the Patent Office as being unpatentable over the art which taught the use of gelatin as a retarding agent. To overcome this rejection, Thompson filed an argument in the Patent Office on June 5, 1952, alleging that gelatin did not act as a retarding agent with ACTH because gelatin with ACTH "causes a sudden and immediate strong response, and in addition, a response which is greater at any point on the curve than that caused by an identical dose of

(*Continued on page 99*)

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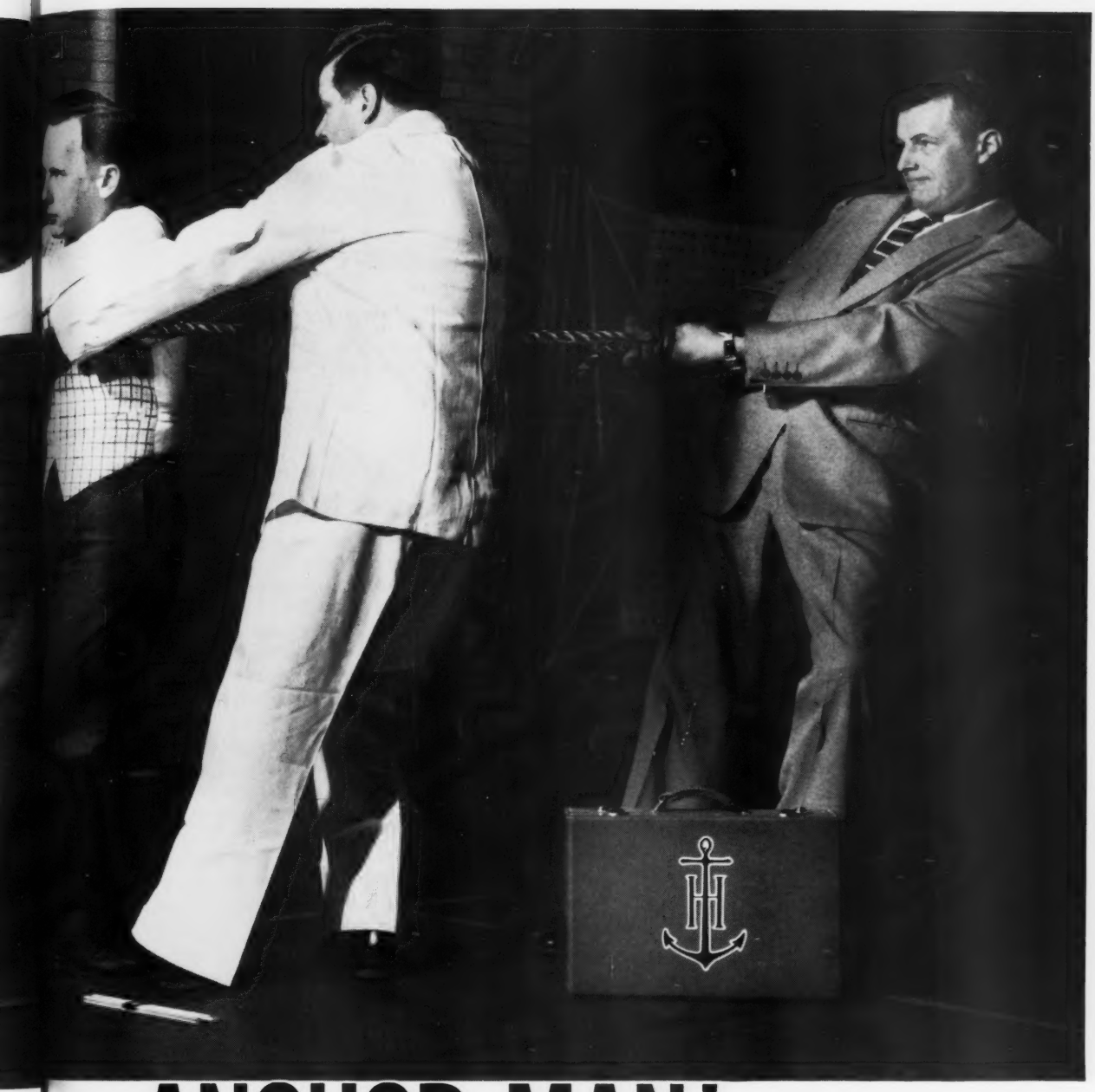

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Announcement is made that

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have combined their interests and will operate as divisions of a New York parent company to be known as

International Flavors & Fragrances Inc.

The identities of these two long-established firms will be retained and each will continue to serve its customers in the same manner as in the past.

By operating in conjunction with each other, they will have development, manufacturing and distributional facilities in fifteen countries, through wholly-owned subsidiaries in North and South America, Europe, the United Kingdom and South Africa.

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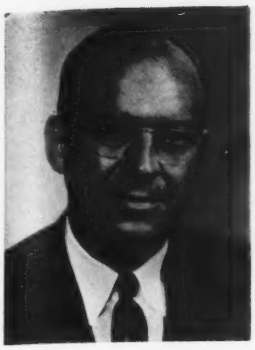

DONALD K. BALLMAN

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BERNARD BERK

GUSTAV CARSCH

NEWS...

Appointments and Promotions

Dr. E. O. Barstow of *The Dow Chemical Company*, Midland, has been named honorary chairman of the board of directors, having retired as regular member of that board, and is expected to attend many meetings in an advisory capacity. Also retired from the board, R. L. Curtis, Dow, San Francisco, who continues as vice-president and a senior officer on the West Coast. Donald K. Ballman, director of sales, and C. B. Branch, manager of the plastics department, replace the two directors. Leland A. Doan, assistant general manager of the *Western Division* since 1955, replaces Mr. Curtis as general manager of that division.

Dr. Bernard Berk, associate technical director of the Overseas Division, Squibb, has been appointed director of the Steroid Preparative Laboratory of the *Squibb Institute for Medical Research*.

Sterling L. Boyce has been promoted from assistant export manager to export manager of *Ayerst Laboratories*.

Paul E. Carman, most recently executive director of research, *S. E. Massengill Company*, has been named vice president in charge of scientific relations.

Gustav Carsch has been named vice president of *Capulco, Inc.*

H. Schuyler Cole has been elected to the board of directors of *Procter & Gamble Company*. He has served as vice-president of the company's toilet goods division and, additionally, has been responsible for managing the paper products division since 1957. Charles M. Fullgraf has been promoted from associate manager of that division to the position of manager.

W. Roger Cooper, long associated with the Latin American export field, has been appointed director of the *Export Advertising Division* of the *Norwich Pharmacal Company*. Drs. Sidney Goldstein and Ivan Stern have been appointed senior research pharmacologist and senior research biochemist, respectively.

Dr. Kenneth O. Courtney, who until recently has served as representative in Brazil for the Pan American Sanitary Bureau and the Regional Office, in the Americas, of the World Health Organization, has been appointed to the medical staff of the department of clinical investigation, *Parke, Davis & Company*.

Frank M. Folsom, chairman of the executive committee of the board of the Radio Corporation of America, has been elected a director of *Crown Cork and Seal Company, Inc.* Other changes at Crown: Everett B. Webster, Secretary-treasurer; Al B. Sheen, export sales manager; Giinther R. Ludwig, manager of closure sales; and Alfred L. Hartung, manager of can sales for the Mid-West sales region.

Seaton Gales, previously sales promotion manager, *Glenbrook Laboratories*, has been appointed assistant to the firm's executive vice-president. Frank W. Millard, formerly assistant sales promotion manager, succeeds Mr. Gales.

J. A. Gibernau, formerly head of the export department, Ames Company, has become director of *Armour Pharmaceutical International*, succeeding S. B. Bradshaw, who is now assistant to the company's president.

Louis Greenberg has been appointed assistant controller of the *Purdue Frederick Company*. He was formerly market analyst for the Pharmaceutical Research Center.

Dr. Albert Hemming, medical director with the Geigy Corporation, has been appointed director of promotion for *Geigy Pharmaceuticals*, a division of the corporation.

John Hilldring, formerly president, was elected chairman of the board of directors of *General Aniline & Film Corporation*. Philip M. Dinkins, who has been vice-president, general manager of the Dyestuff & Chemical Division, was named president.

Appointed to fill the new openings created by *Parke, Davis & Company's* establishment of two new Canadian branches are E. G. Kington, formerly in charge of the Edmonton branch, now manager, the new Vancouver branch; C. A. Rogers, formerly field manager for the Edmonton branch, now Edmonton Branch manager; and Howard Robbins, another former field manager, now manager of the Winnipeg branch. Frank A. Kehrig has been promoted from branch house manager in Montreal to assistant manager in charge of internal operations for the firm's Toronto branch, and Herbert T. McQuade has become Canadian branch house manager. Mr. McQuade was formerly assistant to the Toronto branch manager.

Further appointments, in Detroit, announced by Parke, Davis are: Drs. Mervin E. Brokke and Paul L. Creger to the research staff; Drs. Fred P. Hauck, Jr., and Peter Wing Kee Woo as associate research chemists; Dr. G. Thomas Truffelli as an associate research microbiologist; Barbara J. May, Frances Joyce Mumford and Barbara A. Underwood as research assistants in microbiology;

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ISOPROPYLANS – a series of liquid emollients containing 33% to 50% lanolin. For aerosol-packaged cosmetic preparations – see Product Bulletin 45

LANAMINE – a substituted alkyl amine of selected lanolic acids. For shampoos, shaving soaps – see Product Bulletin 25

LANOGELS – a series of water-soluble polyoxyalkylene lanolins. For shampoos, hair conditioners, lotions – see Product Bulletin 46

LANOGENE – a liquid lanolin fraction. Emollient and plasticizer for hair sets, lotions, lipsticks – see Product Bulletin 28

LANOSOL – a colloidal suspension of pure lanolin. For anhydrous liquid preparations with high lanolin content – see Product Bulletin 48

Product Bulletins on Request.

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Judith L. DeWese, Mrs. Joan E. Garbarino, Mrs. Karen G. Holappa and Barbara L. Whiting as research assistants in Pharmacology; and Mary H. Jones and Fern Probstmeyer as assistant research microbiologists in cancer research.

Frederick C. Kull, senior bacteriologist at *Ciba Pharmaceutical Products, Inc.*, has been appointed director of virology.

A. N. LaBelle has been elected a vice-president of *B. T. Babbitt, Inc.*, in charge of the *Charles Antell Division*, which Babbitt recently purchased. Mr. LaBelle was formerly director of sales, the Lambert-Hudnut Division, Warner-Lambert Pharmaceutical Company.

Kenneth M. Leghorn, formerly president of the Bradley Container Corporation, has been named vice-president and general manager in charge of the newly consolidated *Bradley-Sun Division* of *American Can Company*. Joseph D. Martin, previously president of Sun Tube Corporation, has been made a vice-president of the new division.

Daniel B. McAfee, previously New England district manager for American Cyanamid's Plastics and Resins Division, has been named vice-president in charge of sales for *A. H. Wirz, Inc.* Robert Mahan, who has been associated with Wirz since 1939, most recently as general manager of the Carrollton, Kentucky plant, has become vice-president in charge of operations.

Dr. Wilbur McKellin has been appointed director of organic research for the *Arner Company*. Dr. McKellin formerly served in research with the American Cyanamid Company. Donald A. Kane has been appointed senior industrial engineer.

John T. McLoughlin has joined *Mead Johnson & Company*, the Nutritional and Pharmaceutical Division, as vice-president for market development planning. He was formerly vice-president and assistant to the president of Esterbrook Pen Company.

Hoffmann-La Roche, Inc. has appointed Raymond D. McMurray to the newly created post of general counsel. He was previously with William S. Merrell Company as secretary and general counsel.

Albert W. Merck has been appointed assistant to the executive vice-president of *Merck & Company, Inc.* He was formerly director of advertising and promotion of the Merck Chemical Division.

George R. Moore, formerly with the Owens-Illinois Glass Company, has joined the *Hazel-Atlas Glass Division* of *Continental Can Company* as manager of the division plant at Clarksburg, West Virginia.

Drs. John R. Nazy and Ronald A. Thursack have joined the development department of *Union Carbide Chemicals Company*, division of *Union Carbide Corporation.*

Dr. Robert Ottke, previously with Charles Pfizer & Company, Inc., has been appointed director of commercial development of the *Wallerstein Company, Inc.*

American Cyanamid Company has appointed Dr. R. P. Parker assistant general manager of the *Lederle Laboratories Division.* He was formerly general manager of the Research Division, now renamed the Central Research Division. D. M. Benjamin, previously general manager of the Lederle Laboratories Division, has become general manager of the *Manufacturing Services Division.*

Al Pillet has joined the sales force of *George Lueders & Company, Inc.*

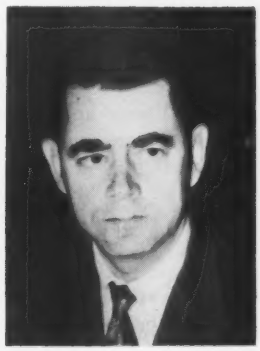
Thomas B. Potter has been named administrative assistant to the vice-

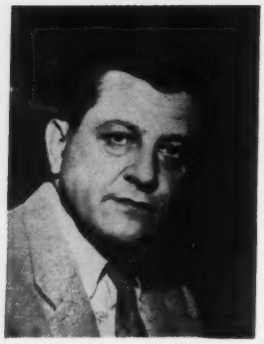
ROBERT C. OTTKE

R. B. PARKER

THOMAS B. POTTER

JOHN G. POWERS





MARVIN STEINBOCK

KENNETH G. VOORHEES, JR.

ROBERT H. WOODWARD

president-sales of the *Commercial Solvents Corporation*. This marks his return to Commercial Solvents after serving for two years as secretary and assistant treasurer, Northwest Nitro-Chemicals, Ltd., a Canadian affiliate.

John G. Powers has been named manager of the newly established *Chemical Division* of *Markem Machine Company*. Bernard Toomey and Douglas Treat are his assistants.

John W. Richardson, a *Parke, Davis & Company* sales representative, has been appointed assistant to the director of the firm's department of clinical investigation.

Efrain Rodriguez has been appointed president and general manager of *Merck Sharp & Dohme de Mexico S.A. de C. V.*, Mexican subsidiary of Merck & Company, Inc. Mr. Rodriguez was formerly field operations assistant for the Latin American area for Merck Sharp & Dohme International.

Cyrus P. Schoen, formerly regional medical representative of Pfizer Laboratories, has joined the *Professional Division, Thos. Leeming & Company, Inc.*

Bryant Pharmaceutical Corporation has announced the following promotions: Nathan Skop, from production manager to plant supervisor, and Alfred Appell, from chief chemist to production manager. Robert Bass and Mrs. Olga Kekish have joined the technical staff of the Control Laboratories, and Edward Weinstein has been appointed internal sales supervisor and coordinator of domestic sales.

Raymond S. Snyder, associated with *Johnson & Johnson* for 22 years, has been named director of national accounts.

William R. Spurlock has been elected to the newly created office of vice-president and assistant to the president of *Eli Lilly Company*. Succeeding Mr. Spurlock as executive director of merchandising operations is James E. Koffenberger, who has been an administrative assistant to the president. William R. Hutchinson has been named director of sales for the firm's east-central region, succeeding the late Walter E. Nelson, who died last November. Mr. Hutchinson was administrative assistant to Lilly's vice-president in charge of marketing.

Frank L. Stamberg has been appointed assistant to the president of *Vick Chemical Company*. He was formerly assistant to the president of Matchabelli-Seaforth, division of Vick, recently sold to Chesebrough-Pond's.

Joel B. Stein, formerly an account executive with Grey Advertising, Inc., has been appointed assistant to the advertising director of *Pharmaceuticals, Inc.*

Marvin Steinbock has been appointed director of production of *Aerosol Techniques, Inc.* He formerly served as vice-president in charge of manufacturing for Powr Pak-ConnChem.

Robert U. Sternfels has been appointed manager of the *Fresno (California) Drug Division, McKesson & Robbins, Inc.* He has been with the firm since 1947, most recently as sales manager of the St. Louis Drug Division. Mr. Sternfels succeeds Tad M. White, recently appointed district vice-president, northwest district. W. Delbert Hill has been promoted to sales manager of the *Kansas City Drug Division.*

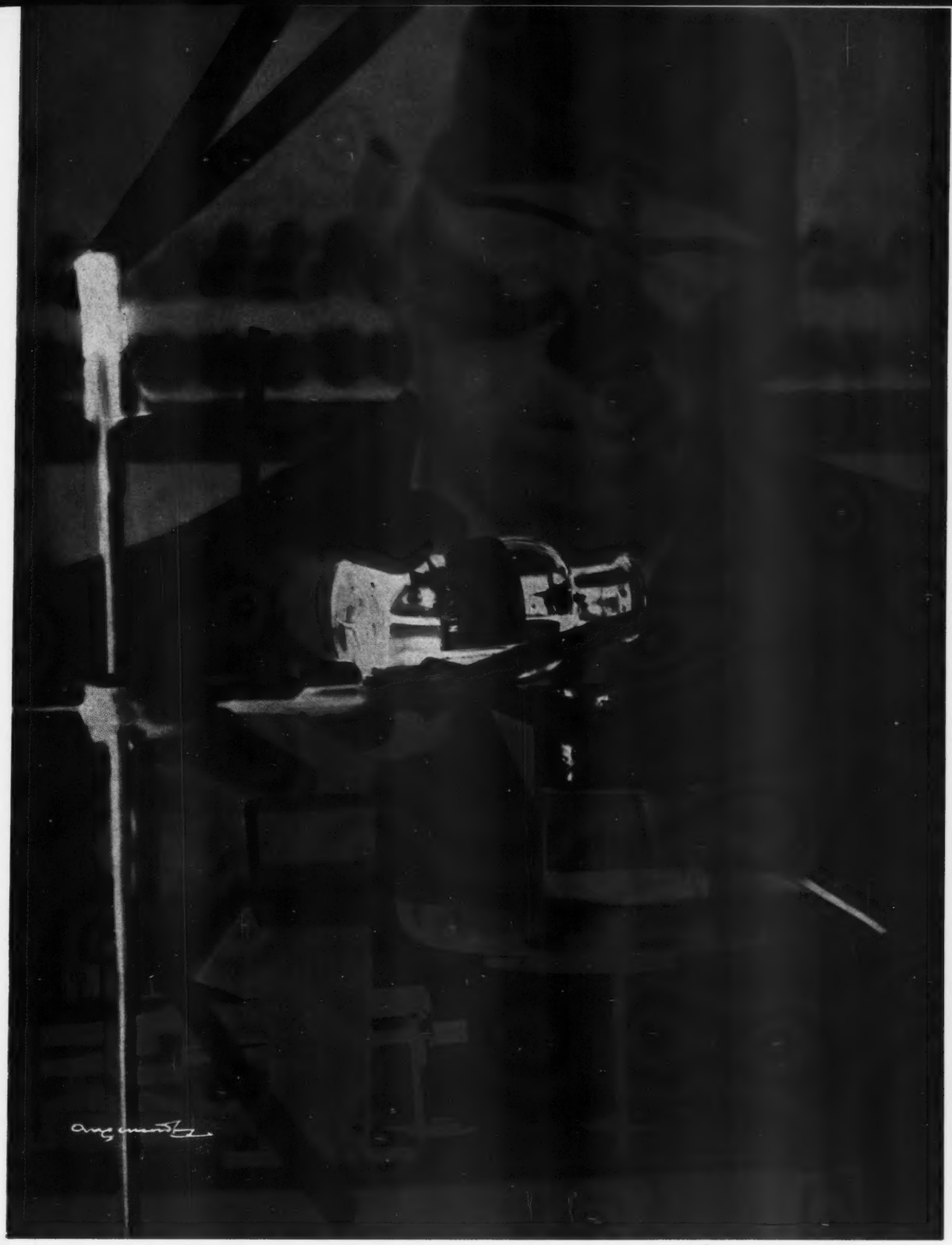
Seymour A. Taylor has joined *Purepac Corporation* as merchandising manager. He was formerly with Chas. Pfizer & Company as marketing manager for proprietary drug products and product manager for ethical prescription products.

Joseph H. Trapold, formerly associate professor of pharmacology at Louisian State University School of Medicine and consultant to the Veterans Administration, has been appointed director of *Sandoz Pharmacology Laboratory* in Hanover, N. J.

Principal officers of the newly formed company, *International Flavors & Fragrances Inc.*, through the merging of van Ameringen-Haebler, Inc. and Polak & Schwarz N. V. are: A. L. van Ameringen, chairman of the board; Charles P. Walker, president; C. C. Brummer, executive vice president; Alolph Schwartz and Waldo F. Reis, vice-presidents. Mr. van van Ameringen, Mr. Walker and Mr. Reis previously held these same positions with van Ameringen-Haebler, and Mr. Brummer and Mr. Schwarz served as managing directors of Polak & Schwarz.

Dr. Manfred Schach von Wittenau has joined *Chas. Pfizer & Co., Inc.* as research chemist in the Chemical Research and Development department, Brooklyn. Dr. Robert B. Stebbins, formerly a research associate in pathology with Merck Institute, for Therapeutic Research, has been appointed a pathologist, and Louis A. Mulieri, an electrical engineer at the Macrobiology department at the Maywood, N. J. laboratories.

Kenneth "Garry" Voorhees, Jr. has joined the staff of *Ungerer & Company, Inc.*, having recently served with the U. S. Armed Forces. Mr. Voorhees is a great-grandson of W. P. Ungerer, founder of the company in 1893, a grandson of F. H. Ungerer and the son of the president, Kenneth G. Voorhees. Prior to his service in the Army, Mr. Voorhees spent considerable time in several manufacturing departments in



Exploring the Secrets of Nature

Applying new scientific knowledge to develop synthetic aromatics hitherto unknown
Re-creating, synthetically, precious natural distillates and extracts
*These are problems successfully mastered * by our research chemists and perfumers.*
Experiences thus gained inspire to further DRAGOCO ACHIEVEMENTS

***BULGARYOL** synthetic Bulgarian rose oil
NEROLYOL synthetic Neroli oil big. pet.
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BRANCHES IN OTHER PRINCIPAL CITIES OF THE U.S.A. AND THROUGHOUT THE WORLD

Ungerer's Totowa plant.

Dr. Alan R. Wagner, formerly with the Research and Development department of the American Cyanamid Company, has joined the new pathology department of *Warren-Teed Products Company*.

Andre Wick, associated for 38 years with *Houbigant, Inc.*, both here and abroad, has announced his resignation as president of the three companies in this group, and assumed the chairmanship of the boards. Succeeding his as presidents are Jacques Manoha, Houbigant, Inc. and *Cheramy, Inc.*, and Gerard Bungener for *Houbigant Sales Corporation*. Pierre Harang, vice-president of the latter company, has been elected to similar posts in the other two companies. V. Vassilieff, treasurer, has also become vice-president of Houbigant Sales Corporation.

Robert H. Woodward, formerly president of Lloyd Brothers, Inc., has been named assistant to the president of *Wm. S. Merrell Company*, division of Vick Chemical Company.

FDA's A. H. Holland Joins Enloe

Dr. Albert H. Holland, Jr., has arranged to purchase a substantial stock interest in the firm of Cortez F. Enloe, Inc., New York, medical advertising agency and consultant to the drug industry. Dr. Holland has been elected executive vice-president and member of the board of directors, and will be the chief operating officer of the agency. Dr. Enloe will continue as president and chairman of the board and as chief executive officer of the firm.

ALBERT H. HOLLAND, JR.

Dr. Holland has announced his resignation as medical director and chief medical officer of the Food and Drug Administration, and is taking up his new duties this month.

A. L. VAN AMERINGEN

C. C. BRUMMER

International Flavors & Fragrances, Inc. Formed

Announcement has been made by A. L. van Ameringen, chairman of the fifty-year-old firm van Ameringen-Haebler, Inc., New York, and C. C. Brummer, managing director of the seventy-year-old firm Polak & Schwarz N. V. Zaandam, Holland, that the two companies merged their operations as of December 31, 1958.

A parent company to be known as International Flavors & Fragrances Inc., with headquarters in New York, provides an organization of first-rank size and broad international scope. Through its wholly owned manufacturing subsidiaries in 15 countries, International Flavors & Fragrances will supply on a world-wide basis fragrance materials for use in products such as perfumes, soaps, cosmetics and aerosols, and flavors for candy, drug, food, beverage and other industries. The van Ameringen-Haebler and Polak & Schwarz organizations will retain their identities as divisions of the parent company. Each will continue to serve its customers as in the past.

The combining of the facilities of these firms is of special importance to both U. S. and foreign-based companies that manufacture and sell abroad through overseas branches and subsidiaries, since the problems of importing materials are becoming increasingly complicated by tariffs, currency restrictions and import licenses. Through the new organization, the overseas producer will be able to obtain materials manufactured locally in key areas throughout the world.

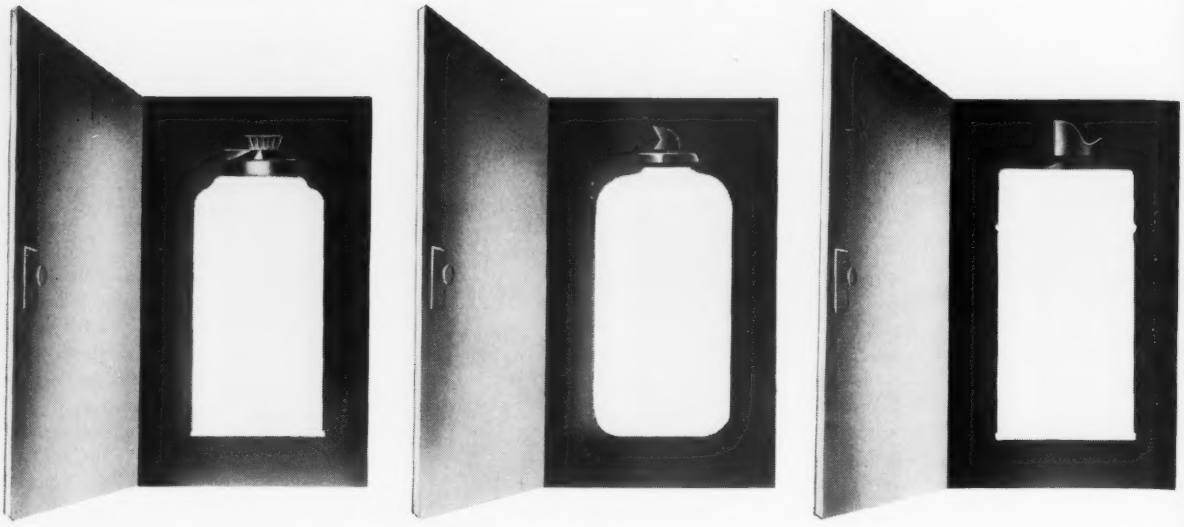
van Ameringen-Haebler has recently completed a 1.5 million dollar expansion of its manufacturing and research operations at Union Beach, New Jersey. It is producing annually more than 2.5 million pounds of perfume materials to meet the growing need for finer fragrances in many kinds of products.

Polak & Schwarz brings to International Flavors & Fragrances a worldwide manufacturing and distributing organization which has been expanding since 1889. Today it operates manufacturing units in 15 countries, with more than 100 agents throughout the world.

In commenting on the merger, Mr. van Ameringen said, "Although both companies are creators and producers of synthetic as well as natural fragrances and flavors, their activities in the past have been largely complementary rather than competitive in terms of products, processes, research and the geographical location of plant facilities. Both companies have established reputations for pioneering work in chemical research and for utilizing modern production techniques. van Ameringen-Haebler has devoted a higher percentage of its efforts to aromatics and fragrances; Polak & Schwarz, on the other hand, has concentrated much of its effort on aromatics and flavors. We look forward to a combined, creative research and production organization better able to serve customers wherever they may be located."

Principal officers of International Flavors & Fragrances, Inc., are: A. L. van Ameringen, chairman of the board; Charles P. Walker, president; C. C. Brummer, executive vice-president; Adolph Schwarz and Waldo F. Reis, vice-presidents. Mr. van Ameringen, Mr. Walker and Mr. Reis previously held these same positions with van Ameringen-Haebler, and Mr. Brummer and Mr. Schwarz served as managing directors of Polak & Schwarz.

Opening New Doors



Aerosol Sprays

CONTAINING

NEOMYCIN GRAMICIDIN TYROTHRICIN BACITRACIN

The use of these antibiotics adds *new product sales appeal* and contributes to *product improvement* in items such as:

Complexion Creams	**Shaving Creams**
Lotions	**Antiseptics**
Sun Tan Oils	**Proprietaries**
Shampoos	**Drug Products**
Deodorants	**Other Specialities**

The recent growth of aerosols for these uses has been outstanding. If you are anticipating a new product or wish to create new consumer demand for your present product, this modern and increasingly popular method may well be the answer. We will welcome the opportunity to work with you. Of course, all discussions will be held in strictest confidence.

PENICK

Manufacturers of Fine Chemicals and Drugs

S. B. PENICK & COMPANY 100 CHURCH ST., NEW YORK 8 • 735 W. DIVISION ST., CHICAGO 10

Institute Elects L. A. Sweet

Dr. Leon A. Sweet, vice-president and director, Parke, Davis & Company, has been elected to the board of trustees of the Detroit Institute of Cancer Research for a three-year term.

Z. O. Moore Elected by Proprietary Association

Z. O. Moore, vice-president, Chattanooga Medicine Company, has been elected to the executive committee of the Proprietary Association, to complete the term of the late Lupton Patten.

ACS Division Elects Cavallito

Dr. Chester J. Cavallito, director of research, Irwin, Neisler & Company, has been elected chairman of the American Chemical Society's Division of Medicinal Chemistry for 1959. He succeeds Dr. Robert M. Herbst, professor of chemistry at Michigan State University.

Perfumers Honor Guenther

Dr. Ernest Guenther, vice president and technical director of Fritzsche Brothers, was recently honored by the American Society of Perfumers at a dinner meeting at the Advertising Club in New York City.

The bronze plaque presented to him by the Society's president, Jacques Masson, manager of Flam-Haft Laboratories, was inscribed: Presented by the American Society of Perfumers to its esteemed member Dr. Ernest Guenther for his outstanding work in furthering the knowledge of essential oils so vital to the science and art of perfumery.

King Chosen by MCA

James F. King has been named assistant to the president in charge of government relations for the Manufacturing Chemists' Association, Inc. Mr. King, who has held a number of advisory and administrative positions in the U. S. Government, came to the MCA after serving as assistant to the director of the Office of Civil Defense and Mobilization. He succeeds Claude E. Hobbs, MCA staff counsel, who has accepted a position in private industry.

Award to Rovesti

Dr. Paolo Rovesti has received the Giuliana Brambilia International Prize in Esthetics and Cosmetology for 1958 in recognition of his work in cosmetics. Dr. Rovesti of Milan, president of both the Italian Society of Cosmetology and the Italian Society of Dermopharmacy, has published extensively on essential oils, vegetable tissue extracts and cosmetic raw materials.

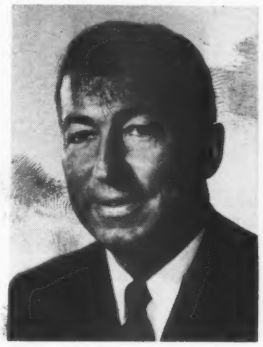
Givaudan Honors 25-Year Veterans

During the annual Christmas party of Givaudan-Delawanna, Inc., held at the Swiss Chalet, Rochelle Park, N. J., some 350 of the firm's employees witnessed the presentation of gold Swiss watches to six new 25-year veterans: Stephen Braun, Theodore Estes, Alphonse T. Fiore, Matthew Sadecki, John Wutsch and Miss Silvia Boggiano, who was not present.

E. R. Durrer, president, H. F. Duffy, treasurer, and Dr. Max Luthy, vice-president, production and research, addressed the group, who were treated to a steak dinner followed by music and dancing.

Arch Elected President

The Chicago Drug and Chemical Association has elected Charles E. Arch president of the association for 1959. Mr. Arch is vice-president of Sheffield Tube Corporation and midwestern sales manager.



CHARLES E. ARCH

Forrest M. Luckett, Monsanto Chemical Company, was elected first vice-president; Samuel A. Davis, C. P. Hall Co., second vice-president; Charles A. Rowell, Walgren Company, secretary; J. C. Browning, DeMert & Dougherty, Inc., treasurer.

John de Elorza Joins YPO

John de Elorza, president of Old Empire, Incorporated, has been elected to the Young Presidents' Organization, a group which consists of presidents of corporations doing business in excess of one million dollars and who have attained presidencies prior to their fortieth year.

Old Empire, Inc., are manufacturing chemists packaging and manufacturing aerosols, perfumes, drugs and cosmetics for private brands. Mr. de Elorza has designed and developed many specialties.

Dr. Ernest Guenther, Fritzsche Brothers, receiving a bronze plaque [illegible] in essential oils [illegible] president of the American Society of Perfumers.

E. R. Durrer, president, Givaudan-Delawanna, Inc., presenting gold Swiss watches to veterans of 25 years with the firm during the recent Christmas party [illegible] Rochelle Park, N. J., left to right: Stephen Braun; Theodore Estes; [illegible] F. Duffy; [illegible] Alphonse T. Fiore; Mr. Durrer; Matthew Sadecki; John Wutsch; and Dr. Max Luthy, V.P. of production.

ROCHE* VITAMIN B_6

Be sure your products

have the **PROPER PYRIDOXINE CONTENT**

Increasing interest among MDs

The value of pyridoxine is receiving increased attention from physicians. The symposium on "Newer Vitamins" held under the auspices of the National Vitamin Foundation at Vanderbilt University summarized research work and pointed the way to new fields of investigation. As a result, doctors and diet experts are giving more study to the importance of the vitamin to health and nutrition.

Metabolic imbalance in pregnancy

Pyridoxine's particular place in the metabolism of tryptophane and other amino acids may be significant in correcting certain metabolic imbalances known to exist in some pregnancies.

Important in infant feeding

Already proven vital in infant feeding, new evidence suggests that it may be important in preventing some congenital malformations.

ALL-TIME NEW LOW PRICE

Now is the time to re-examine your products in relation to proper pyridoxine content. Feel free to call on Roche for technical assistance. Our staff is always ready to help.

Quick reasons for your choice of Pyridoxine, U. S. P. Roche

Quality—Equals or exceeds U.S.P. standards. May be used for Rx parenterals.
Uses—Ideal for all types of pharmaceutical formulations and dietary supplements.
Supply—Need a gram . . . or a ton? Roche will supply you.
Delivery—Strategically located warehouses insure fast service.
Packaging—Polyethylene bags sealed with saf-t-tag. In ½ and 1 kilo tamperpruf metal containers. Larger quantities in fibre drums; small in amber, screw-cap bottles.
Samples?—Ask your Roche salesman or write the Vitamin Division.

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Call **ROCHE** *for VITAMINS*

Vitamin Division • **HOFFMANN-LA ROCHE INC.** • Nutley 10, N. J.
NUtley 2-5000 • New York City: OXford 5-1400
Pacific Coast distributor: L. H. BUTCHER Company • San Francisco • Los Angeles • Seattle • Portland • Salt Lake City
In Canada: Hoffmann-La Roche Ltd., 1956 Bourdon Street, St. Laurent, P. Q.

Testagar Takes over Fellows Co.

The Fellows Medical Manufacturing Company has moved its complete operation from New York City to 1354 W. Lafayette, Detroit, headquarters of Testagar & Company, which has taken over the complete operation, including the manufacturing and executive staff.

Sid Heinrick, president of Testagar has also assumed the posts of general manager and treasurer of the Fellows Company, and both firms will operate from the same address in Detroit.

Raiser Re-elected by NPC

Carl K. Raiser, director of distribution, Smith Kline & French Laboratories, has been re-elected president of the National Pharmaceutical Council.

Others elected and re-elected officers are: Newell Stewart, executive vice-president; Nelson M. Gampfer, board chairman, Wm. S. Merrell Company, Paul Gerdon, secretary and general counsel, Abbott Laboratories, Henry S. McNeil, president, McNeil Laboratories, Inc., and George W. Orr, Jr., president, Ames Company, Inc., all vice presidents.

Also re-elected were Wilbur E. Powers, secretary; L. J. Sichel, vice-president and counsel, Ciba Pharmaceutical Products, Inc., treasurer; and Franklin P. O'Brien, vice-president, G. D. Searle & Company, executive committee chairman.

In his keynote address, Mr. Raiser said that the workings of pharmaceutical manufacturing would be explained to pharmacy school professors of administration at a new, week-long seminar to take place in August, 1959 at the Princeton Inn, Princeton, N. J.

National Pharmaceutical Council President Carl K. Raiser (center) discussing plans for his forthcoming year's program with president-elect Howard C. Newton (left) and president Louis J. Fischl of the American Pharmaceutical Association.

Parke, Davis Opens California Office

Parke, Davis & Company recently began operations in its new branch office in Menlo Park, Calif.

The branch is headquarters for all Parke-Davis operations in northern California, western Nevada and Hawaii. G. Carl Tasker is branch manager.

Dow Opens Carolina Office

The Dow Chemical Company is opening a sales office at 504 Wachovia Bank Building, Charlotte, North Carolina, as of February first, covering North and South Carolina and parts of Virginia and Tennessee.

New Kohnstamm Flavor Plant

A new H. Kohnstamm & Company flavoring plant was recently dedicated at Kearney, New Jersey. Covering an area of 40,000 square feet, the plant is designed for a continuous flow of production, from raw materials to finished product.

New Armour Sales HQ

Marketing and sales promotion executives of the Armour Pharmaceutical Company have moved to the Prudential Building in Chicago. The new address is Prudential Plaza, Chicago 1; the telephone, MIchigan 2-1611.

Penick Moves Offices

The general offices of S. B. Penick & Company and its New York Quinine & Chemical Works Division has moved to 100 Church Street, New York City 8. Telephone numbers remain the same. The teletype number for both Penick and NYQ is TWX NY 1-3461.

Dr. E. G. Klarmann, vice-president and manager, technical services, Lehn & Fink Products Corp., receiving the Chemical Specialties Manufacturers Association Achievement Award from James Ferris, CSMA president.

ACS Chooses A. L. Elder

Dr. Albert L. Elder, director of research of the Corn Products Company, has been chosen president-elect of the American Chemical Society for 1960. Dr. John C. Bailar, Jr., professor of inorganic chemistry, U. of Illinois, is president for 1959.

Fritzsche Honors Stebbins

For the seventh time this year, the Quarter-of-a-Century Club of Fritzsche Brothers, Inc., has met to honor a new member, this time, Frank J. Stebbins. The firm's officers and directors feted him at a luncheon and presented him with a large denomination Government bond and a scroll. Mr. Stebbins also received, from his co-workers in the sales division, a stereophonic hi-fi set.

Hughes Receives Wellcome Prize

Lieutenant Colonel Carl Wilson Hughes, M.C., U.S.A., was awarded the Wellcome Prize at the annual convention of the Association of Military Surgeons for his essay, "Vascular Surgery in the Armed Forces." The prize is a silver medal, a scroll and an honorarium of $500, and it is presented annually for the best essay on medico-military affairs prepared by one of its members.

PAC Elects Audrey Girard

Mrs. Audrey Girard, advertising manager of J. B. Roerig & Company, has been elected secretary and a director of the Pharmaceutical Advertising Club. She is the first woman director and officer in the 500-member organization's 25-year history.

HIGH SCORING PROTECTIVE COLLOID

VEEGUM® scores high with Cosmetic and Pharmaceutical Manufacturers because it does so many jobs so well. VEEGUM is a natural inorganic thickener, emulsion stabilizer and suspending agent. VEEGUM is purified magnesium aluminum silicate, with thixotropic properties. It is non-toxic and non-irritating. It is odorless and tasteless, white and opaque.

USED IN AQUEOUS DISPERSIONS:

VEEGUM suspends at lower viscosities than organic gums.

VEEGUM, being thixotropic, gives long-time stability.

VEEGUM, thickening slightly with heat, keeps product consistency uniform despite above normal storage temperatures.

Why not try VEEGUM in your laboratory? We'd be delighted to send samples.

Use This Coupon To Get Fast Action

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230 PARK AVENUE, NEW YORK 17, N. Y.

( ) Please send VEEGUM Bulletin 53J ( ) Send sample of VEEGUM

State Application _____

Name _____

Title _____

(Please attach coupon to your Company letterhead) P–2

Kolmar Laboratories To Make Products Available in Peru

In order to make Kolmar Laboratories or customer's products available in Peru and surrounding countries, negotiations are in process with laboratories Leonard S. A. of Lima under which Kolmar production should be available soon for distribution there.

Merck Opens Atlanta Branch

A new branch has been opened in Atlanta, Ga., by Merck & Co., Inc., at 3415 Empire Boulevard, with J. B. Vandigriff as manager.

Whittaker, Clark Relocates

Whittaker, Clark & Daniels, Inc., has announced the relocation of the company's New York office at 100 Church Street.

Babbit Purchases Antell

B. T. Babbit, Inc., has signed an agreement for cash for the assets, trade names and trademarks of Charles Antell, including the Canadian concern, Charles Antell, Ltd.

A. N. LaBelle, formerly director of sales with Lambert-Hudnut, has been elected a vice-president of Babbit in charge of the new Charles Antell Division.

Eastman Chemicals Division Opens New Southern Offices

The Chemicals Division of Eastman Chemical Products, Inc., subsidiary of Eastman Kodak Company, has established new sales offices for its industrial and specialty chemicals in Atlanta, Ga., and Greensboro, N. C.

The former, located at 3133 Maple Drive, N. E., Atlanta, will be headed by Jack T. Mahaffey, representing Eastman in Georgia, Florida, Alabama, Mississippi and Tennessee. Richard Fayssoux is assigned to the Greensboro office, in the Jefferson Standard Building, representing the firm in Virginia and North and South Carolina.

Snyder Tool & Engineering Changes Name to Snyder Corp.

The Snyder Tool & Engineering Corporation, parent company of the Arthur Colton Company, has changed its name to the Snyder Corporation, to avoid misconceptions concerning the type of equipment it manufactures.

Parke, Davis Opens Two Canadian Branches

Parke, Davis & Company, Ltd., has announced the establishment of two new Canadian branches, one in Vancouver, British Columbia, with E. G. Kington as manager, and one in Winnipeg, with Howard Robbins as manager. Mr. Kington was formerly in charge of the Edmonton branch, and Mr. Robbins has been field manager of the Edmonton branch. C. A. Rogers becomes Edmonton branch manager.

American Can Consolidates

The American Can Company has consolidated the operations of its two former subsidiaries, Sun Tube Corporation and Bradley Container Corporation, with the parent company, to be known as the Bradley-Sun Division.

Kenneth M. Leghorn, formerly president of Bradley Container, has been named vice-president and general manager, and Joseph D. Martin, previously president of Sun Tube, has been made a vice-president of the new division.

Manufacturing operations will be continued as in the past at the former Bradley plant in Maynard, Mass. and the Sun Tube plants in New Jersey.

Markem Establishes Chemical Division

The Markem Machine Company has announced the establishment of a Chemical Division with John G. Powers as manager, to be assisted by Bernard Toomey and Douglas Treat. The division will be responsible for sales and service of Markem machines to the chemical, cosmetic, paint and varnish, and drug and pharmaceutical industries.

French Pharmaceutical Service Opens New York Office

Droit Et Pharmacie, French pharmaceutical consulting service, has extended its operations to include an international division with representatives in the U. S., Italy, Germany and the Benelux countries.

Legal advice and visa applications for new drugs top the list of services offered, which also include an information bulletin.

The U. S. office, managed by Mrs. Erna Engle, is located at 305 Broadway, New York 7, telephone, DI 9-0654.

Aureomycin Plant in Canada

American Cyanamid Company has announced that construction will soon begin on Canada's first Aureomycin chlortetracycline plant, as an addition to the production facilities of its subsidiary Cyanamid of Canada, Limited. The new facilities are at the site of the present plant between Niagara Falls and Welland, Ontario. Aureomycin will now be manufactured entirely in Canada for Canadian customers.

Dome Chemicals Moves

Dome Chemicals, Inc., has moved to larger quarters at 125 West End Avenue, New York City. Besides modern automated laboratories, the new quarters include a doctors room for visiting physicians.

Howell R. Jordan

Howell R. Jordan, second vice-president and member of the council of the American Pharmaceutical Association, died on January 7 at Austin, Texas. He joined the Association in 1938 and served as treasurer for one term, as president of the board for two terms. At the time of his death he was operating in partnership two exclusive prescription pharmacies and four other retail pharmacies.

Lupton Patten

Lupton Patten, president of Chattanooga Medicine Company and past president of the Proprietary Association, died on December 7, 1958 at his home in Chattanooga, Tenn.

Mr. Patten at the time of his death was a member of the Association's executive committee and had been for many years.

Archibald L. Ross

Archibald L. (Larry) Ross, vice-president in charge of sales, Wyeth International, Ltd., Inc., died suddenly on December 16 at his home in Rosemont, Penna. Mr. Ross was 44 years old.

Ralph C. Jennings

Ralph C. Jennings, midwestern agent for the New York Quinine & Chemical Works Division of S. B. Penick & Company, died January 7, in Chicago. He had been associated with NYQ for more than 50 years, having served as a vice-president when McKesson & Robbins owned the firm.

Management Forum

BY FRANCIS CHILSON
INDUSTRIAL CONSULTANT

Rejuvenating A Failing Company

The first step to take in revitalizing a business that has been sliding is to fire Mr. Big, the president. This isn't as simple as it sounds especially when Mr. Big and his family—own or control a substantial block of stock. Everyone likes to feel he is a good administrator even when he is confronted year after year with the financial results of his poor stewardship. Everyone likes the self important feeling of being on top. So strong is this conceit that there are some men who would let their company go to hell before they would voluntarily place the tiller in more competent hands. They would let it go to hell even though they owned all the stocks themselves. Rare is the man who willingly will accept blame and abide the consequences.

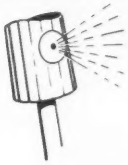
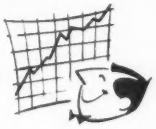
When a company goes sour Mr. Big *must* bear the blame. He is responsible for executing the policies of the board of directors, and, more often than not it is the president himself who sets the policies and sells them to the Board. All too often many members of the Board are, in operational matters, the president's subordinates and they don't dare oppose him overtly, because, if they do they had better begin looking for other jobs!

Parenthetically it may be said that few boards of directors are worth a fiddler's damn. Some are composed of nonentities and exist only as legal formalities. Some are composed mainly of bankers who know nothing about industry but everything about money. Some of them are composed in the main of the president's subordinates; his 'yes' men, playboys, and socialites whom Mr. Big wishes to impress in the hope of enhancing his own social standing. Every board should have, of course, members who are thoroughly informed on banking and finance, taxes, law, public relations and economics. Thus you have a banker or investment broker, a tax expert, a lawyer, a public relations man and an economist. Add perhaps one or two men who know the industry intimately and you have a board that can be enormously helpful. This is of course only an ideal because first class men in the specialties enumerated are interested only in the larger companies. But even a small company can use an ideal as a standard of measurement of the men available to it.

But to get back to Mr. Big whom we have just fired. Sometimes it may be impolitic to fire him outright; in such cases he can be promoted to Chairman of the Board. I once succeeded in persuading the president of a company I was reorganizing to step down in favor of his associate. Since the gentleman in question owned thirty per cent of the stock in the company this took a bit of salesmanship and a bit of pressure internal and external. But the company then broke is now a very profitable operation. In this case the president was a first rate scientist, who had the illusion he was also a first rate business administrator. This is a very common illusion among scientists.

The next step in the rejuvenation process is to prune the staff to get rid of the deadwood. Every organization has deadwood, even those that have reputations for high efficiency. The pruning process is painful because in so many cases it should have been done so long before, when the company had no moral responsibility toward the individual. But when a dead duck has been allowed to float along for ten or twenty years, the company does have a moral duty because no effort was made either to develop the individual or to get rid of him if it appeared that he lacked development potential. Now when the company is in a financial jam it can't fulfill its moral obligations but if it is to survive, the deadwood must ruthlessly be cut out. The pruning process is indeed painful because it raises hell in the community. Everyone blames the company. And the company *is* to blame. Thirty years ago in this column I advocated an annual personnel audit to prevent the accumulation of

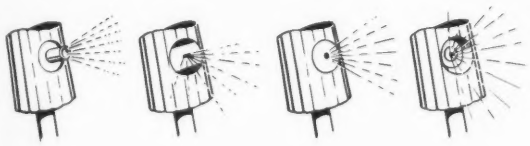
A Thirty Second Success Story

Once Upon A a happy Aerosol man wanted to be more successful. His product was good, but not selling as smoothly or as much as he wanted. Then he got just the he needed for increased success! "I'll try the Quality Newman-Green Aerosol Valves  and see if their exclusive features really do help  profits."

Sure enough, it worked! Production went smoother, customers were assured of more dependable dispersing, And His Profits Went Up! Now he has more to relax and enjoy his fishing or bowling—all because he insists on the exclusive found only in Newman-Green Aerosol Valves.

You can be just as successful. Contact your nearest Newman-Green representative today for complete details and the new price sheets.

Four typical spray tips, all interchangeable in seconds.



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It would be a pleasure to send you our new price schedules and valve samples. Simply fill in the coupon below and mail to:

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Name_____

Address_____ State (Country)_____

Company_____ Title_____

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Cosmetics are the leading sales producers right now and pharmaceuticals will make the next big market . . . Why? . . . The big buyer of merchandise will buy the items that are easy to operate, are not messy and require no guess work.
Aerosols are the answer and Precision's great laboratory has developed a stream, metered stream, drop or metered drop for such cosmetic products as hand creams, lotions, hair creams, facial creams, depilatories, and for the new market of pharmaceuticals in aerosols, such as vitamins, antibiotics, dietetic sweeteners, cough medicines, tonics.
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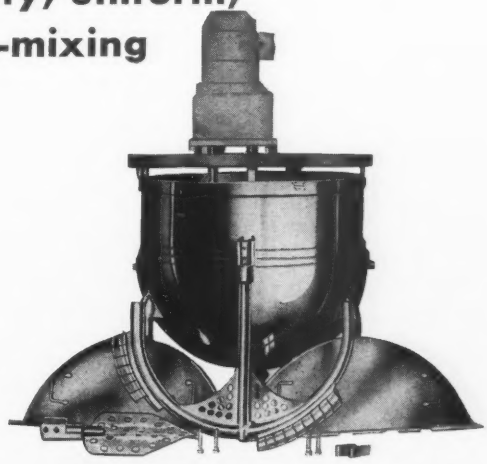
Nothing could be finer

GROEN stainless steel, steam-jacketed, COOKER-MIXERS for high purity, uniform, dependable blending-mixing

Whatever your cooking-mixing-cooling operation, look to GROEN for your stainless steel, steam-jacketed "cooker-mixer" kettles designed to process virtually any viscous product to exacting requirements. They're available in stationary and trunnion designs, for any capacity required.

Pictured here, the Model TA stationary kettle features twin-shaft agitator assuring thorough blending-mixing. Main agitator with finger-like scraper blades rotates slowly and swirls the material into the high-speed, secondary mixer. Design permits the use of various mixers—paddle, beater, bar or turbine types. All agitator parts can be easily removed for fast, effortless cleaning.

GROEN also builds a complete line of stainless steel Mixing, Cooking and Storage Tanks, Revolving/Coating Pans, and Vacuum/Pressure Vessels. For more technical information and engineering counsel, write to Dept. DCI-159.



GROEN MODEL TA stainless steel "cooker-mixer" kettles are ideal in processing creams, batters, adhesives, pigments and other viscous materials. Laboratory and pilot plant models are also available.

Extra heavy-duty, lifetime construction plus sanitary, modern design.

GROEN REVOLVING PANS

Dependable, silent-operating, stainless steel, Revolving/Coating Pans (with or without steam-jacket) are available in a wide range of bowl diameters—pitched for maximum capacity. Motor and drive are completely enclosed.

FREE LITERATURE

Bulletin TAK-2 gives complete description and specifications on GROEN line of stainless steel, stationary and trunnion "cooker-mixer" kettles. Revolving/Coating Pans described in Bulletin VP-1. Literature sent on request.

World's Largest Producers of Stainless Steel, Steam-Jacketed Kettles —Since 1907

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deadwood in all eschelons and to prevent the accumulation of a moral responsibility for people who are not doing their jobs as they should be done and who, perforce, are incapable of handling greater responsibilities than they already have.

Since a business cannot operate without an organization the selection and indoctrination of competent individuals to replace the deadwood is not an easy task. If the company has been sliding for some years the fact is known in the trade and it is a difficult job to persuade good men to take a chance on a dying company. But sincerity and evidence of sufficient capital to carry on plus money, a title and stock participation or substantial percentage bonuses will work wonders as bait.

The key man of course is the president. He's the team leader. Since the drug and the cosmetic industries are *selling* industries he should either be a first rate marketing man, or, a man who has had extensive contact with marketing organization and procedures, and of course he should be also a good administrator. Usually a first rate marketing man is a good organizer, a good practical psychologist with an instinctive understanding of men and motives. Where he is weak in other administrative requirements he can be supported by specialists or consultants.

The next man of importance in the process of reorganization is the salesmanager or the director of marketing. Regardless of the competence of the president in marketing, his other administrative duties will prevent his giving the full attention to marketing *in the field* that this vital operation requires. He has to have a leg man.

No moribund company can be reorganized from the bottom up; it must be reorganized from the top down. The process of reorganization never ceases. As a company grows and diversifies, changes in organization are necessary to meet new conditions. But I am talking here of the dying company. It cannot be shored up from the bottom and it is futile to expect that it can be led uphill by the same men who led it down.

At this time I shall not explore further other important functions of organization. I have concentrated on the keys to the log jam. Now let's talk about the log jam itself—the line of products the company is offering the trade.

The drug industry in particular offers a market for a various and extensive list of products. In spite of all the publicity all the miracle drugs lumped together: antibiotics, vitamins tranquillizers, hormones, sedatives etc. account for about a third of the total ethical drug business. Not every firm has a miracle drug. No firm can afford to wait until its research department comes up with one. It must sell what it has. But it cannot sell everything. No firm in this industry has ever been large enough or diverse enough to supply the wants of the trade even though some firms,—the physician's supply houses and the so-called "service houses" had from four to six thousand items in their catalogues. Their catalogues were almost as big as the old fashioned family bible.

No firm can supply all things for all people. So a line must be drawn that will permit concentration on those items which with reasonable sales effort will show the greatest profit result. This means rigorous pruning of the line. When a company is losing money it is difficult to persuade the management to drop items that are bringing in dollars no matter how few. There is a widespread illusion that a few thousand dollars of sales income on a bookkeeping basis makes a potential contribution to profit, whereas it usually does actually the opposite. On a bookkeeping basis an item that sells for a four time mark up looks profitable—many people think it *has* to make a profit —but if it doesn't sell in substantial quantities and if in the line there are many other similar items, the effect is to increase overhead enormously in every-phase of the business and at the same time, such items decrease the efficiency of the sales department to a substantial extent.

No salesman can do a worthwhile selling job on an extensive line of piddling items. He will concentrate on one of those items for which there is some demand and everything else can go to the devil. Salesmanagers set weekly or monthly quotas of slow moving items. A dozen items this month; a different dozen next month until they've gone through the catalogue. When a few items are given a hard push for a while there may be a languid response but the moment the pressure is diverted the items go dead again and the druggist curses himself for falling for the gimmick or deal that caused him to buy the stuff. For years Rexall has followed this practice in selling proprietaries on a national scale. Periodically a group of staple proprietaries and cosmetics is offered at what amounts to half price, the gimmick being that the normal price is not cut but the customer gets two items for an additional penny.

The law of diminishing returns applies to the line of products carried by every firm: the more items in the line, the more overhead entailed, hence a lower profit. If any.

Let me now apply what we've outlined here to an actual case in which I personally participated in 1936 —Sharp & Dohme. In that year Sharp & Dohme was a sick company. For most of the years since the merger with Mulford in 1928 the company had operated very slightly in the black or altogether in the red and it had not paid a dividend since the merger. Market opinion of the company was indicated by the fact that its stock was offered at $4. per common stock share. For a short period it actually dropped to $2. At that time S&D's catalogue contained 4200 items!

Here's how the three procedures outlined above were applied. Remember: fire the president, prune the staff, prune the line.

The old president was fired, that is to say he "retired," and Jack Zinsser was appointed president. As soon as he sized up the problem I was retained to reorganize and modernize the factory in the hope of reducing costs to reasonable proportions. The staff was pruned. As I recall something like 170 people of all ranks from vice president down were dropped—most of them in the factory. New people were brought in but not many. Zinsser was smart enough to make the best use of the talent and experience that he had available. There were many changes and consolidations during the first year but the toughest nut to crack was to persuade the sales department to prune the line.

At that time ten per cent of the company's annual sales volume of ten million dollars was in private label and private formula business. Something like three thousand private formulae were made and the company would accept a private formula order for three thousand coated tablets! In retrospect such a thing seems impossible but it is a fact. I saw at once that the company was losing money on almost every private formula order it handled and had studies mades to prove it. But when I proposed to the management that the whole private business be dropped at once, the sales department then under Hugh Long, landed on me like a ton of brick. Throw away ten per cent of their dollar volume in a depression period? I must be nuts! When I produced figures to show they were losing money on private work, the sales people argued that private work helped to absorb overhead; it helped to sell S&D products—in fact if certain private formulae weren't made for certain hospitals, they would stop buying S&D products. And so on ad infinitum. I then began to analyze the amount of S&D products bought by private label customers and the amount was so small that I was shocked to realize that salesmen could kid themselves to that extent. When I put the facts before Zinsser he issued an edict and that was the beginning of the end of the private business. At the same time a kill committee was instituted to cull out their own line.

These steps taken in time marked the beginning of the upturn of Sharp and Dohme which has continued ever since and is still continuing under the aegis of Merck & Co.

Revolutionary Coating Process

The Wisconsin Alumni Research Foundation has invented a revolutionary technique and apparatus for coating tablets in a minute fraction of the time normally required. Twenty minutes as against three days! The process consists of keeping the tablets suspended in an upward moving air stream while the coating materials are atomized directly on them. This may sound implausible to you but I have inspected a variety of tablets coated by this method and the coatings are remarkably uniform. WARF intends to license under their patents and I am going out to Madison next week to investigate the process further. I will have more details for you next month. This is the first revolutionary approach to the coating operation in a century. I am very keen on it because I prepared a design in 1946 for a horizontal tumbler in which the coating materials were injected into a moving air stream. More anon.

Stock Earnings

The market performance of drugs stocks has been remarkable during the past year. I happen to be drug consultant for one of the big funds and I urged the purchase of substantially more drug stock over a year ago. The bankers were cautious. Drugs stocks already were too high; they were at the top of the price—earnings ratio; besides there are the impending antibiotic price fixing suits. The situation didn't look rosy. As a matter of fact they advised me to sell a lot of my drug stock and diversify. So I compromised. I sold most of my miscellaneous holdings and bought drug stocks. So now when I go to a meeting down in Wall Street, I sit there with a smug grin on my puss, which the financial analysts think is most revolting. The rise in the market is an overwhelming vote of confidence in the drug industry on the part of the public. The public expects us to keep up the performance of the past ten years. If we fail to do so the wave will fall as high as it rose.

Thought For 1959

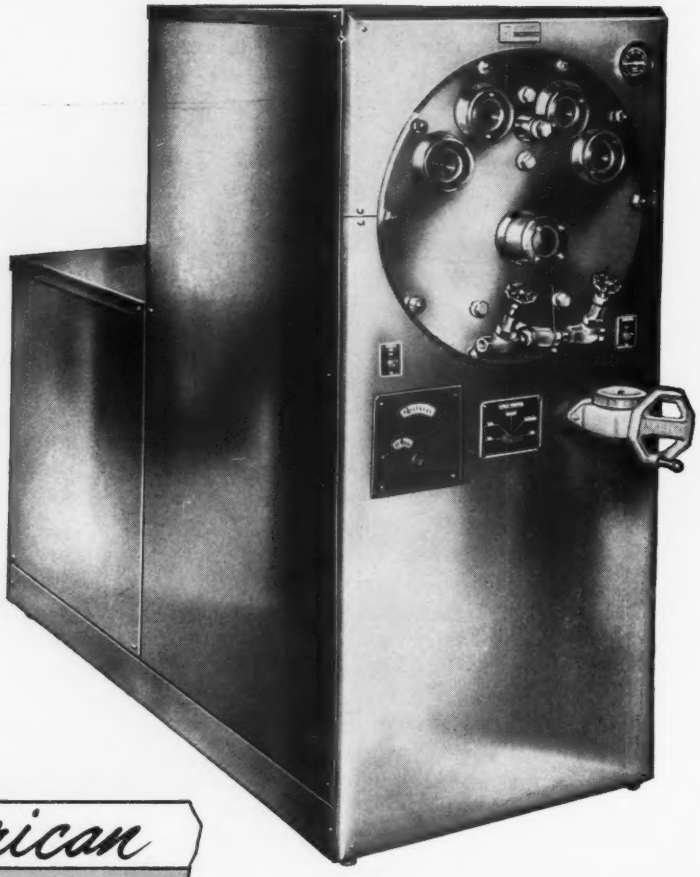
In these troubled times I have found from my reading of history two comforting constants: The first one is, that the good old days were always the best. The second is, the younger generation is going straight to hell.

Thinlite

The subjoined letter from my good friend Ben Dennis, Jr., V.P. of Kimble Glass division of Owens-Illinois, Toledo, Ohio, briefly discusses O-W Thinlite, a remarkable construction glass product for curtain walling and also Toplite panels for roof lighting. These new developments are remarkable for strength, construction simplicity, thermal efficiency and glare control. As soon as I get through digesting the 427 pages of data Ben sent me I'll have something to say further about these outstanding new developments. In the meantime if you have ants in your pants write directly to Ben. (*Go to it Junior!*)

"Dear Frank:

"Your comments in one of my favorite magazines are always interesting to me and usually incline me toward composing a letter to you. As you know, I resist that temptation in most instances, for I know you are very busy and really can't take the time to read the thousands of letters you get from your readers. What you have to say, however, in the September issue under the subject of "Research Goldfish



American BIOGEN *for* CONTINUOUS CULTURE OF MICROORGANISMS . . . IN LARGE QUANTITIES

● Biogen is a completely new apparatus which produces extremely large quantities of specific microorganisms quickly, economically and continuously, under well defined conditions.

For the first time, vastly increased investigations requiring large populations of microbial cells become fully practical in such diverse fields as Bacterial Physiology, Enzymology, Genetics, Pharmacology, Fermentation Studies, and Virology (including Bacteriophage).

The Biogen is self-sterilizing and has complete controls on the front panel which govern the sterilization cycle, rotation of the multi-finned agitator and the temperature within the chamber. Chamber temperature is maintained at $\pm\frac{1}{2}$° C. within a range of 20° C. to 85° C. A filtered air intake provides sterile aeration of the medium within the chamber.

In a recent typical run, with *E. coli B* employing 1% glucose as the limiting growth factor, a maximum population of 1.68×10^{10}/ml. was attained. In 10 hours, on a continuous process, at a flow rate of 10 liters/hour, 14 grams/liter of wet weight cells were harvested. Total yield for the 10-hour run: 1400 grams.

Write for technical literature . . . Bulletin IC-605

AMSCO

AMERICAN STERILIZER

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World's largest designer and manufacturer of Sterilizers and Equipment for Biological Research

Bowls" struck me as being so good that I have not been able to resist the temptation to compliment you upon your accomplishment.

"To be perfectly honest, your approach to the matter of glass boxes parallels so closely our views that I am not sure whether we have been smart or highly unoriginal. We do feel, however, that glass properly used can do a perfectly amazing job in bringing the daylight into the interior of buildings through controlling the sunlight that is admitted either through the side walls or through the roof.

"Knowing that you are always willing to learn something new, I thought that you might be willing to glance through the literature that I am sending you in order to see how our Thinlite Curtain Walls make it possible properly to light the interior of rooms with daylight, or through the use of our Toplite bring in controlled daylight through panels in the roof. The Hillsdale High School is a rather amazing plant, in that the majority of the classrooms are interior rooms but they are so beautifully lighted by means of our Toplite Panels that the atmosphere is very conducive to study and concentration.

"I am sure it won't make you mad to know that one of your constant readers took the time to send his greetings and best wishes.

Cordially,
Ben Dennis"

Drinking

Liquor is the most ancient of tranquilizers. In one form or another it is consumed by almost every race of people on earth and in the past tense by those under it. It is undoubtedly true that man could make liquor before he could make fire. How could he make fire without a little liquor in him? Consider the number of hotel fires in our time that are caused by people going to bed with a load on, with lighted cigarettes more or less firmly clenched in their lips.

One of the interesting observations I have made about this delicious-pernicious habit is that the man who habitually drinks most resents it in other people. He's the first to say that every time he goes into Gilhooley's Bar, Joe Doakes is always there. It never occurs to him that the observation makes the score even both ways. When the salesman smelling of liquor call upon a customer, he rarely gets an order even though the customer has just got back from a late lunch and has half a load on himself. The customer and the salesman may go out on the town together but that's a different matter. The moral is: never call on a customer or a client smelling of liquor because the customer, even if he is as full as a jug, will resent being reminded of the fact that he is in a position where he can't immediately get a drink himself.

On the subject of drinking my good friend Dr. Irvine Grote of Chattanooga is probably the world's outstanding authority. If he drank one hundreth part of the liquors in his collection he'd also be the world's outstanding drunk. He has a collection of countless thousands of whiskies, wines, liquors and cordials from all over the world. He even has a sample of a Chinese cordial which contains the corpse of a poisonous snake. This proves that the Chinese are smarter than we are because they see the snake actually before they drink the stuff; therefore when later on they see other snakes, as we often do, they don't get alarmed or froth at the mouth; they know they are not real.

Granulation Costs Avoided With Use of Reheis Lump $Al(OH)_3$ Gel

According to reports released here recently by the Reheis Company, Inc., its lump form, dried aluminum hydroxide gel is being used successfully to eliminate the costly and time consuming granulation step in the preparation of tablets. This makes possible the dry mixing of incompatible formulas that previously could not be made into ordinary tablet form.

"Lump form $Al(OH)_3$ gel is produced already possessing the extra density needed for such operations. Its excellent stability also provides easier handling. With the lump form gel (Reheis type F-2000) dry mixing can be utilized in a wider range of formulas that can ordinary dried gels. It can easily reduce lump F-2000 to the right screen size to suit his particular formula," a Reheis spokesman commented.

Meeting USP XV standards, Reheis lump form, aluminum hydroxide gel carries the same price schedule established for the regular dried F-2000 gel.

For additional information write: The Reheis Company, Inc., Berkeley Heights, N. J.

Disposable Pre-Sterilized Petri Dishes

Fisher Scientific Co. now offer crystal clear molded polystyrene Petri dishes that are pre-sterilized. They claim the dishes are priced so low that it is now cheaper to use them once, throw them away than to wash glass dishes.

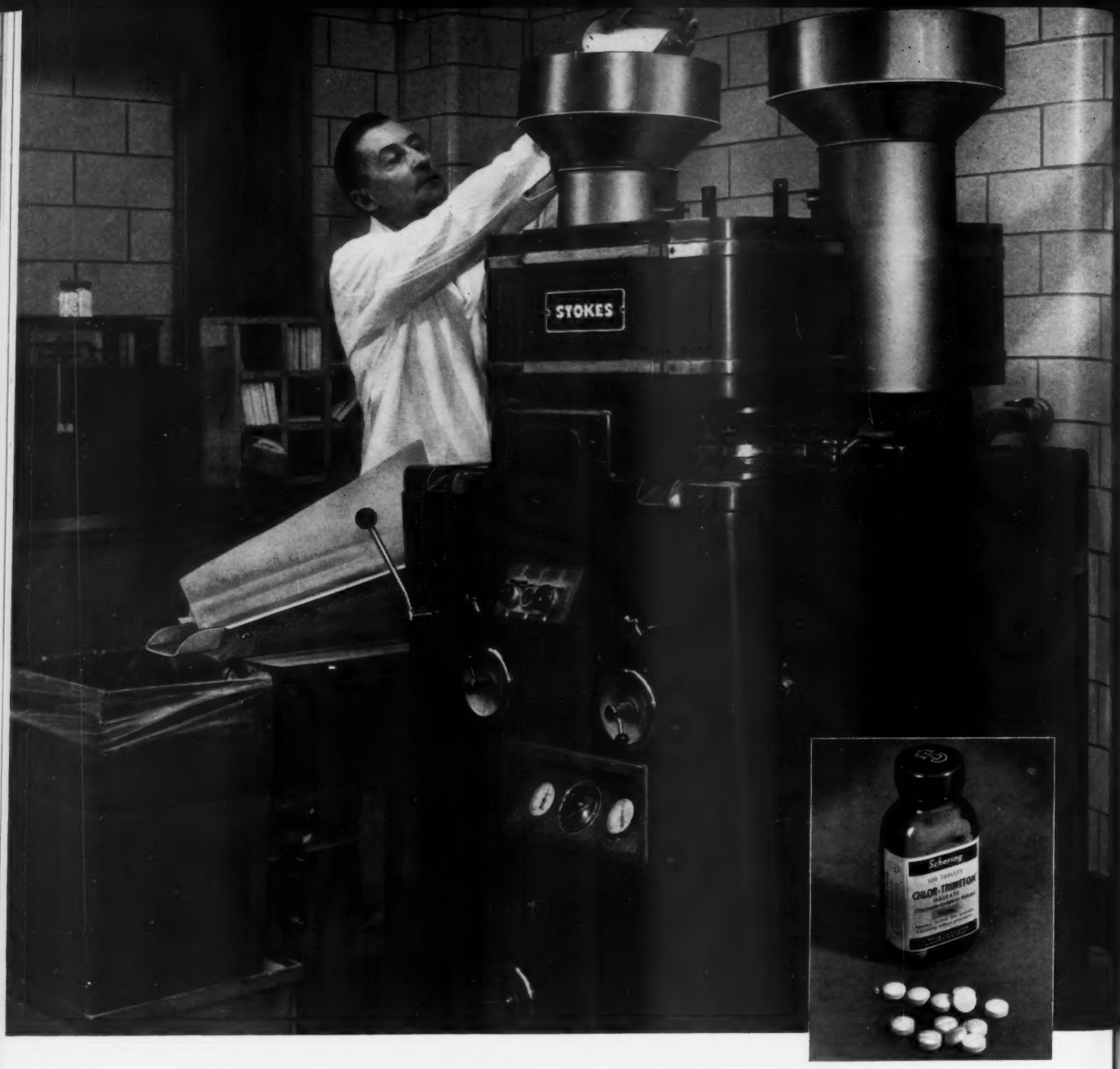
The dishes are available in round, square, radial grid, square grid, bi-plate and tri-plate models.

Aerosol Can Disposal & Product Reclaiming Device

A device for reclaiming the contents and disposing of the empty aerosol can has been developed by the Builders Products Co. of 108-110 Wooster St., New York 12, N. Y.

Empty Aerosol Can Packer

A new empty aerosol can packer is now available from Emhart Mfging Company's Portland, Conn. Div. Handling two cases at a time, the new Standard-Knapp packer economically, and without chipping or scratching, speeds seven-ounce or 12-ounce containers through the line at the rate of 240 cans per minute in a 3 x 4 x 1 pattern. Changing over grid and pusher plates takes but 15 minutes.



OTHER STOKES EQUIPMENT AT WORK FOR SCHERING . . .

Schering uses a Stokes 566 Multi-layer Tabletting Machine for perfection in multi-layer tablets. Stokes exclusive layer pre-compression permits periodic weight checks—gives clean, sharp separations.

Part of a bank of Stokes Polishing and Coating Pans at Schering. Here, standard Stokes machines have been neatly built into a custom installation behind gleaming stainless steel panels fitted with glass doors.

Operator Kenneth W. Shaw fills the hopper of one of the Stokes high speed Model 540's at Schering. This 41 station machine produces many Schering products, such as Chlor-Trimeton-Maleate, at rates in the order of 3000 tablets per minute.

Accuracy is important and is checked often at Schering. The centralized control area provides constant visual indication of speed and pressure at the punches. Single hydraulic release control permits absolute tablet uniformity from both compression stations of the double sided Model 540.

Dependable high-speed production for Schering...with Stokes pharmaceutical equipment

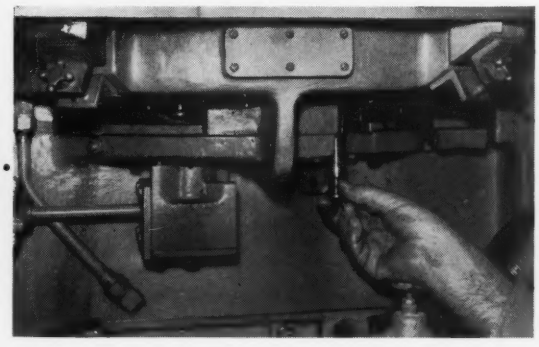
Schering Corporation, Union, New Jersey, demands maximum reliability, efficiency and speed in producing their broad line of steroid hormones and other pharmaceutical products—both ethical and over-the-counter.

Schering's tabletting operation depends on Stokes equipment. Most recently installed are two Model 540 Rotary Tabletting Machines that are in constant operation 16 hours a day, 5 and 6 days a week, manufacturing a variety of drug products. Chlor-Trimeton-Maleate anti-histamine and anti-allergic formula, for example, is produced at speeds up to 3000 per minute. These tablets are 200 mg., imprinted and scored. The high speed and dependability of this operation keeps tabletting costs at their lowest possible level.

Schering takes advantage of the complete line of Stokes pharmaceutical equipment. In addition to operating many Stokes tabletting machines—including conventional and multi-layer—Schering processes their products in Stokes mixers, oscillating granulators, coating pans and polishing heads. And, of course, Schering uses long lived Stokes punches and dies in their tabletting machines.

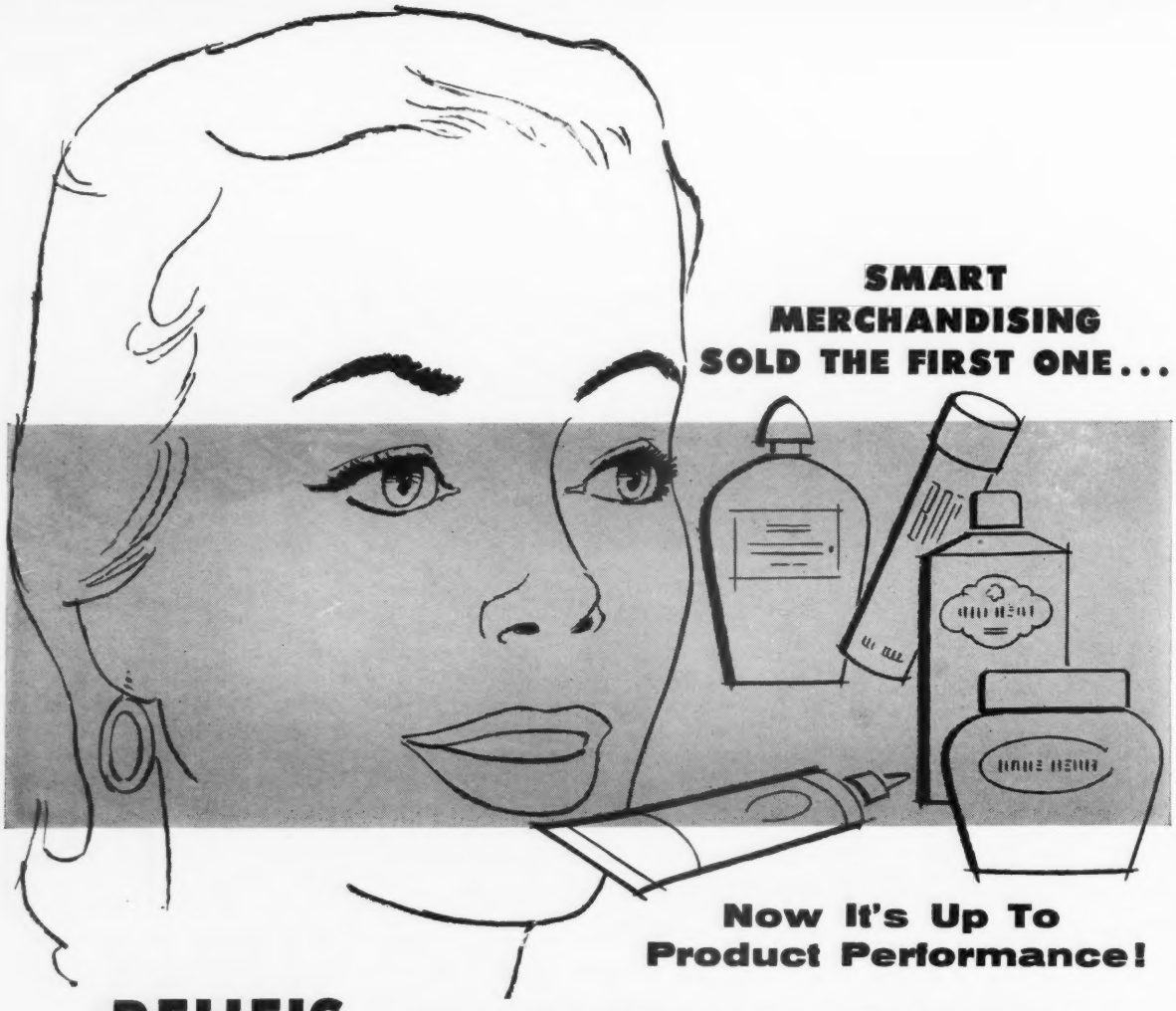
Find out how this advanced design pharmaceutical equipment can save on your own production. Write to Stokes for complete information, or call your nearest Stokes office.

Pharmaceutical Equipment Division
F. J. STOKES CORPORATION
5500 Tabor Road, Philadelphia 20, Pa.



Maintenance problems are small at Schering. Here, the photographer caught the operator changing punches—snapped this picture because it illustrates the ease with which such service is accomplished on the Model 540.

STOKES



SMART MERCHANDISING SOLD THE FIRST ONE...

Now It's Up To Product Performance!

REHEIS ANTI-PERSPIRANT CHEMICALS
give your product all these advantages

Three safe, easily incorporated types insure quality and effectiveness of your product.

For Creams, Lotions, Sprays and Powders: **CHLORHYDROL** (aluminum chlorhydroxide complex). Available in five forms... granular, fine, medium, impalpable, 50% w/w solution.

For Gels: **CHLORHYDROL S-5** (aluminum chlorhydroxide complex—modified). Solid form for grease and gum free alcohol gels.

For Sticks: **CHLORACEL** (sodium aluminum chlorhydroxy lactate complex). Available as a 40% w/w solution for use in making Cologne-type sticks.

In addition, these fine Reheis anti-perspirant chemicals possess astringent properties that recommend them for use in a variety of products for exterior bodily use. Reheis can tailor any of their anti-perspirants to meet the needs of your products. We suggest you write for data and samples... and learn how a quality-grade Reheis chemical can help you keep selling your product.

REHEIS CHLORACEL Anti-perspirant gives *your* products *all* these advantages.

- **Effective anti-perspirant action**
- **Fine deodorant qualities**
- **Non-destructive to fabrics**
- **Non-irritating to skin**
- **No buffering required**

FINE REHEIS CHEMICALS

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Manufacturers of Fine Chemicals
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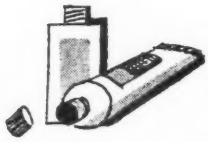


Advancing Therapy

The Steroid Rat Race

Merck and Schering are now busily engaged in advancing dexamethasone as the newest steroid miracle, with greater potency per milligram and, so far, proportionately decreased side-effects. The compound is 9α-fluoro-Δ^1-16α-methylhydrocortisone, a variation of prednisolone in the addition of the 9α-fluoro and 16α-methyl groups. Dexamethasone differs from hydrocortisone in that it contains a Δ^1-double bond and the 9α-fluoro and 16α-methyl substituents. A substantial part of the miracle lies in the near-simultaneity with which the two companies arrived at the same compound. Now Syntex has entered the picture with a new class of potent cortical hormones (H. J. Ringold, O. Mancera, C. Djerassi et al. *J. A. C. S.* 80: 6164, 1958). The most potent in the reported group, with 200 times the anti-inflammatory activity of hydrocortisone and about the same potency as dexamethasone, is the acetate of 6α-chloro-9α-fluoro-16α-hydroxy hydrocortisone-16,17-acetonide. Surely there is many a slip twixt the rat and the human, but research in this steroid field is snowballing, and if a research department expects to get a prior patent position it had better start working on a three-shift basis.

Prolonged-Action Medication

The rush to prepare all sorts of medicaments in some one of the prolonged forms has been so great that one manufacturer taunted his competitors by preparing a long-acting placebo according to C. A. Dragstedt (*J.A.M.A.* 168: 1652, 1958). Most of them fall into two categories: (1) those in which the active drug is coated with some agent more or less resistant to gastric digestion or which dissolves or disintegrates slowly in any fluid (e. g., fats, waxes, fatty acids, shellacs, glycerin esters) and (2) those in which the active drug is adsorbed on an ion-exchange resin from which it is rather slowly eluted. They are marketed in the form of tablets, capsules, and liquid suspensions. Some of them are made in alternating rings of coating material and drug. Still others are prepared by incorporating the drug with sugar pellets or other nuclei, coating these nuclei with varying thicknesses of a selected coating material, and preparing the ultimate dose-form by assembling an appropriate conglomerate of coated and uncoated pellets. The repeat-action product is a preparation in which the two or three doses of the active ingredients that the unit contains are released at two or three presumably predetermined time intervals. The sustained-action product is a preparation which purports to release a portion of the active ingredient relatively promptly and subsequent portions more or less uniformly throughout the ensuing period of 6 to 12 hours.

The advantages claimed for these prolonged forms of medication are obvious. Medication taken once a day instead of two, three, or four times eliminates the inconvenience for the ambulatory patient of taking medication when away from home. A more substantial advantage claimed is that administration of these prolonged forms obviates the peaks and valleys of drug concentration in blood and tisues, which are associated with intermittent administration of ordinary preparations, and enables certain drugs to maintain their effectiveness through the bedtime hours.

Acknowledging the praise-worthy objective of prolonged preparations in certain fields does not, however, necessarily constitute an admission that they achieve this objective in these fields, nor constitute an encouragement to the extension of such preparations in a random or wide-spread manner. Administering a drug preparation by mouth involves many more variables than when it is injected intramuscularly or subcutaneously. It may enter a stomach with or without food, and with or without much gastric juice. It may remain there for widely variable periods of time and then be emptied into an intestinal tract, which also may vary as to the digestive juices with which it accosts the preparation and the celerity with which it transports it to the outside world.

Campbell and co-workers from the Food and Drug Laboratories of Canada have studied what they call the "physiological availability" of drugs in various preparations, by determining the percentages of administered drug that is absorbed.

Their studies are sufficiently convincing to warrant the statement that a preparation which actually succeeds in delaying the disintegration of the administered form, and thereby the absorption of the active ingredient to any dependable degree, inevitably does so at the expense of some loss in precision of dosage.

A number of published reports support the contention that administration of prolonged-type preparations leads to a more prolonged effect than that produced after administering ordinary preparations and/or a more evenly sustained level of drug in the blood. In a few studies, determinations of blood levels have been adequate to establish that there is less "peak and valley" rise and fall in such levels after administration of prolonged-type preparations as compared with ordinary preparations.

No drug whose precision of dosage is important should be administered by a prolonged-type preparation, because a bona fide decrease in disintegration and absorption necessitates an unknown decrease in physiological availability. Drugs whose normal absorption from the gastrointestinal tract is impaired or erratic should not be administered by prolonged-type preparations. The administration of drugs in a prolonged-type preparation should be viewed with misgiving if the total does administered is more than two or three times the usual therapeutic dose, unless the drugs concerned are known to have substantially wide margins of safety between therapeutic and toxic ranges. These restrictions leave a substantial area in which there is reason to anticipate that the employment of prolonged-type preparations should offer advantages over conventional preparations. At present, there is grave disagreement as to the relevance of in vitro tests, with respect to predicting the behavior of prolonged-type preparations when administered to patients.

Vitamin Supplements

Vitamin preparations are used extensively and are valuable when used properly. For the most intelligent use and beneficial results in preventive or therapeutic medicine, the values and the limitations of vitamins should be realized. It is important that a clear differentiation be made between vitamins as dietary supplements and vitamins as therapeutic agents. The Council on Foods and Nutrition of the A.M.A. has reviewed the indications for administration of vitamins in supplemental and therapeutic amounts, the composition and dosage of vitamin preparations, and the possible dangers of excessive use of certain vitamins.

Vitamins are essential nutrients, and their usual source is food. All the nutrients essential to the maintenance of health in the normal individual are supplied by an adequate diet, one which fulfills the Recommended Dietary Allowances, revised 1958, developed by the Food and Nutrition Board, National Research Council (Publication 589). The levels of nutrients recommended are desirable goals in nutrition for all normal, healthy persons.

The Recommended Dietary Allowances should not be confused with the Minimum Daily Requirements established for labeling purposes by the Food and Drug Administration. Nutrient contents can thus be expressed in terms of the proportion of daily requirements supplied. Minimum Daily Requirements are the amounts of nutrients needed to prevent symptoms of deficiency and to provide a small factor of safety. Recommended Dietary Allowances are amounts of nutrients which will maintain good nutrition in essentially all healthy persons.

Healthy persons whose diets are ordinarily considered adequate may benefit from supplementary vitamins at certain special periods of life, such as during pregnancy and lactation. Vitamin supplementation is useful during periods of illness or deranged mode of life, which may result in impairment of absorption of nutrients or deterioration of dietary quality. Supplementation may also be of value to the individual who, through ignorance, poor eating habits, or emotional or physical illness, does not eat an adequate diet.

The daily diet of the artificially fed infant should be supplemented with vitamins C and D if the diet does not supply 30 mg. of vitamin C and 400 U. S. P. units of vitamin D. The diet should be brought up to these amounts, with care exercised that the intake of vitamin D is not excessive.

Healthy adults receiving adequate amounts of wholesome foods need no supplemental vitamins except vitamin D, which should be supplied throughout the growth period.

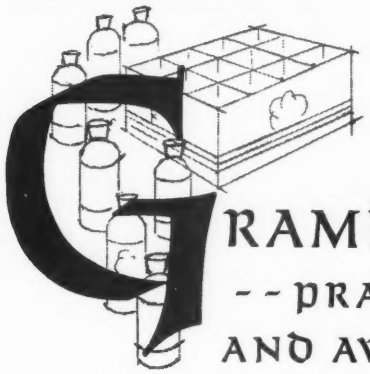
Healthy adults reeciving adequate diets have no need for supplementary vitamins except during pregnancy and lactation when 400 U. S. P. units of vitamin D daily are required if the intake of vitamin D-fortified milk is low. In these periods of physiological stress, if any doubt exists as to the adequacy of the previous or present diet, supplementary vitamins in addition to vitamin D should be administered.

Multiple vitamin preparations should contain only those vitamins shown to be essential in human nutrition or metabolism. The Council recognizes that certain foods such as liver, yeast, and wheat germ are excellent sources of some of the vitamins but finds no evidence to justify special claims for such materials or their concentrates in multivitamin mixtures. The combination of vitamins in a supplementary mixture should have a rational basis.

The multivitamin preparations available today fall into three general categories, those that supply (1) about one-half the Recommended Dietary Allowances, (2) one to one and one-half times the Recommended Dietary Allowances, and (3) three to five times the Recommended Dietary Allowances. The Council considers the first class of preparations useful in dietary supplementation in situations as noted in the section entitled Vitamins as Dietary Supplements. The preparations containing one to one and one-half times the Recommended Dietary Allowances (group 2) would be useful when supplementing therapeutic diets or when prolonged illness or other causes significantly reduce food intake. After the normal diet is instituted, these higher potency preparations are not needed. The third general type of preparations containing three to five times the Recommended Dietary Allowances should be reserved for use in therapy.

Minerals have been combined with vitamins in mixtures for dietary supplementation. Although certain supplemental vitamin mixtures with calcium, iron, or with both minerals have proved useful, there is no good evidence to support the inclusion of the 12 or more mineral elements essential for man. Few of these minerals are likely to be lacking, even in restricted diets. When iron is needed as a dietary supplement, it should be given as such in most instances. Iron and calcium might be included as optional ingredients in certain supplemental vitamin mixtures, for example, for administration during pregnancy. A combination of calcium and vitamin D in stabilized form may be useful. Sodium, chlorine, and iodine are usually supplied by iodized table salt. Supplementation with copper is rarely needed since it is usually adequately supplied by the diet. Evidence is lacking that addition of the trace elements, such as manganese, zinc, cobalt, and molybdenum, to the human diet is needed.

—*J.A.M.A.* 169: 41, 1959.



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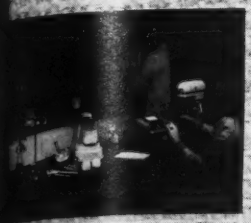

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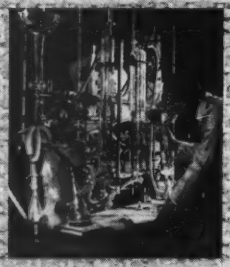

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Perfumer's Shelf

Boronia Fragrance

The brown and gold blooms of *Boronia megastigma* have a rich perfume which is most satisfying according to B. G. Spencer (*S.P.C.* 31: 959, 1958). Very scant mention is given to its odorous components in the literature, and apart from beta ionone only a little appears to be known of the chmeical composition of the fragrance. The natural absolute itself, although a valuable adjunct in many floral and fancy perfumes, is somewhat expensive and does not exactly duplicate the odor of the living flower.

Beta ionone is, of course, the obvious base note, and must be of good quality. Thus the Boronia fragrance can be reasonably recalled by mentioning beta ionone, orange, rose, and thyme. However the normal constituents of orange and orange blossom are apt to upset the Boronia perfume considerably, and a search was necessary to find the ideal aromatic. The answer was found in Jasmonal H, this being needed in large amounts, together with traces of nonyl aldehyde and linalol. The rose effects must be smooth, so rhodinol and phenylethyl methylethyl carbinol were chosen, with excellent results. Phenylethyl methylethyl carbinyl acetate provided a touch of fruitiness without spoiling the composition. Thyme oil must be used sparingly, the concentration not exceeding one half per cent. Traces only of natural oils give the required shading and the whole is rounded off with musks.

Allyl Ionones

To impart interest and life to otherwise flat or undefined fragrance compositions is the chief purpose of the use of allyl ionones. Effective even in minute quantities, allyl ionone requires great care in formulation and careful testing to prevent predominance. Its initial fragrance is of a full, warm, flowery character, the bottom note of the fruity-woody type.

Two grades of allyl ionones are available: the crude grade which contains terpenes and resinoid components is chiefly suited to soap perfuming, and a pure grade. Applications of the purified allyl ionone are the subject of an article by Rochus Martin Classen in *Parfuemerie und Kosmetik*, 1958, No. 11, pp. 748-9.

Flower notes contain the largest amounts of methyl ionone, as in iris, violet, cassia, wallflower, etc. Such florals gain greatly by incorporation of one to two per cent of allyl ionone. In the case of especially delicate notes even these percentages may be too high. Interesting top notes of the fruity type can be obtained by incorporation of 0.5 to two per cent in perfumes intended for hand lotions, face tonics, etc. Up to five per cent of allyl ionone may be added to lavender compositions for improved over all freshness and a fuller and rounder top note. The compound's good compatibility with linalyl acetate enhances spreading power of such lavender type fragrances beyond that of conventional compositions.

The presence of more than five to six per cent of allyl ionone in lavender fragrances results in emphasis on the fruity note. This may create original effects. However, the lavender scent may be transformed into a fancy fragrance merely reminiscent of lavender, and allyl ionone may dominate the terminal odor. Compatibility of allyl ionone with opoponax and orange oils facilitates compounding of interesting lavender compositions of the modern ambrette type.

One to two per cent of allyl ionone in men's perfumes of the woody type make for better definition. Variations on the tobacco theme frequently have a flat top note owing to an excessive amount of tonka products, coumarin, etc. Allyl ionone can be used to lift the top note of such compositions.

Allyl ionone is well suited for use in soap perfumes, where it effectively counteracts the odor of the soap mass and where the freshness of its fragrance is particularly desirable. The boosting power exhibited by allyl ionone even in small amounts facilitates the use in soap of fragrances heretofore considered too delicate or insufficiently stable in this medium. Allyl ionone can widen the range of soap perfumes not only by boosting or supporting other compounds but also as the basic theme in perfume bases intended for this purpose. Such a base might contain as much as 11 per cent of this compound.

Orange Oil Evaluations

In a series of orange oil evaluations two American oils were found to differ substantially in specific weight, refractive index, and distillation residues from values given in the literature, according to E. Benk, *Seifen-Oele-Fette-Wachse*, 1958, No. 12, pp. 367-8. Work is reported on 12 samples of oil of orange peels made by pressing or extraction with highly volatile solvents. Non-volatile constituents varied between 0.96 and 7.76 per cent. In addition to fatty or wax-like components (saponification number 89.8 to 114.8) orange peel oils contain compounds resembling phosphatides. Colors (carotenoids) cannot be demonstrated in all the oils. The tests did not show adulteration by the introduction of foreign material as the cause of the deviations found in the samples of American oils. No evidence of adulterants such as brominated oils was found.

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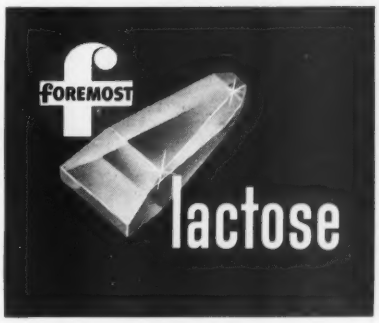

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Compounder's Corner

Silicones for Moisture-Proofing Human Hair

Five different organo-silicones were evaluated as formers of water repellent films on human hair. A combination of acetoxy-silanes and alkyl silicone phosphates was found most promising in work reported by Kurt Weigel in *Seifen-Oele-Fette-Wachse* (pp. 61-2, 1958).

Solutions of methyl silicone of oily consistency in isopropyl alcohol have to be of fairly high concentration to give effective moisture protection and are therefore apt to make the hair excessively oily and streaky.

Siliconates, though good waterproofers in the textile field, present pH problems when applied to the human hair. Their use would have to be followed by application of an acid preparation. Theoretically, the silicone salt could be neutralized with an acid shortly before use. Such a solution would remain stable for a little while. However, to avoid precipitation a certain amount of accuracy and care are required in making the solution and these are not usually available in a beauty parlor.

Methyltrichlorosilane was found to be a very good water repellent, but, used without additives it forms a dull film on the hair which flakes upon brushing. Formulated in low concentrations with softeners and similar substances methyltrichlorosilane gave promising results. However, its application releases small amounts of hydrochloric acid, which though usually harmless to hair and scalp, could conceivably create problems if improperly handled. In addition, it might form white clouds of ammonium chloride by combining with the ammonia vapors which are ever present in the beauty parlor.

Almost equally good water repellency can be accomplished with acetoxysilanes which offer added advantages over the chlorosilanes: not only is the formation of dull film eliminated, but dull hair actually acquires gloss by application of acetoxysilanes This may in part be due to liberated acetic acid.

Among alkyl silicone esters the phosphates are most suitable for moisture proofing human hair. Almost odorless, alkyl silicone phosphates are slightly less efficient water proofers than the acetoxysilanes. Combinations of the two compounds yield very good results. To avoid brittleness of the hair a little silicone oil may be added.

The above conclusions were reached by submitting hair treated with these five types of silicone compounds to four different tests. The strength of wave in set hair was evaluated at different ambient humidity levels by means of weights; tear and tensile strength was measured; thinness and evenness of the film was inspected by micro-projection; and finally the gloss of the coated hair was measured by means of a photoelectric cell. Storage stability tests were included in the studies.

The work cited in this report was performed with pure materials, i.e. with the respective silicone in a suitable solvent in the absence of additives. Softeners, gloss producing agents, and other ingredients can be added for improved results.

Special Ointment Base

A special ointment base made without petrolatum, mineral oil or paraffin wax so that it is quickly and completely absorbable by the skin, has been developed by Martin-Valer Associates of New York. Although anhydrous, the mixture is hydrophilic and is emulsified by aqueous skin secretions. It has been tested on many dermatologic patients with a common denominator of skin dryness, scaling and itching. The ointment was prepared to other anhydrous and emulsified preparations because it relieved itching, penetrated the horny layer, and gave a more lasting suppleness and smoothness to the skin surface. It caused no irritation or sensitivity.

New Cosmetic Materials

The use of esterified protein hydrolysates and of cholesterol amino esters is beneficial to the nitrogen supply of cells in the human skin. Creams containing two per cent of these esters are shown to increase elasticity of the tissues and smoothness of the skin surface, to eliminate small cracks and to cause optimal regeneration. Synthesis of the oil soluble esters and their experimental evaluation are described in an article by Paul Rovesti in *Parfuemerie und Kosmetik*, 1958, No. 10, pp. 707-8. The most valuable esterified proteolysates were derived from connective tissues of the plasma, the blood and the skin, in that order. The best amino acid esters were the lysates of the ethyl esters of histidine and valine.

The following conclusions are reached by the author: Cholesterol esters of essential amino acids and proteolysates esterified with cholesterol constitute a completely new group of starting materials for cosmetics which are of outstanding importance to the correct percutaneous nourishment of the skin. Best results were obtained with protein hydolysates esterified with cholesterol. Second best were the cholesterol aminoesters of hystidine and valine. Percutaneous penetration of all compounds in these groups is unques-

tionably established. If purified as described, they do not cause sensitization, hyperemia, or any other skin lesions. The healing and nourishing effect of the amino esters obtained by the method described is immediate upon application. Functional animation of the skin results in improved appearance.

Improved Bleaching Solution

Activated charcoal in powder form may be added to solutions intended for the removal of color from hair, furs, feathers, etc., according to German patent 1,026,485, Rudolf Bastian, Heppenheim, Germany. Such solutions usually contain reducing agents. Their efficacy is said to be improved considerably by the presence of activated charcoal which is commonly used to decolorize solutions.

Skin Protective Compound

A skin care preparation containing both reducing sugars and amino acids is described in German patent 1,025,101, Chemische Fabrik Promonta G.m.b.H., Hamburg. Usually such preparations incorporate either reducing sugars or one or more amino acids in an aqueous base with or without fatty materials. The simultaneous use and combination of both types of compounds is claimed to lead to deep penetration of the horny layer of the skin, which is thus kept moist and able to perform its natural functions.

Pentoses are the reducing sugars of choice for this purpose. The novel protective cosmetic should contain 5 to 10 per cent of pentoses and two to five per cent of amino acids.

Photo-Protection

A new liquid cosmetic for protection against light is described in *Medizinische Kosmetik*, 1958, No. 7. The preparation is composed of extracts of tormentil, *Malva silvestris* (mallow), and camomile; azulene; a high molecular sulfimide; and lactic acid.

Hair Dye

An aqueous solution of a direct dye is made by first adding an organic solubilizer to the water. This solubilizer must be chemically inert both to the dye and to the hair which is to be dyed. It must also be completely miscible with water, according to French patent No. 1,138,955. The solubilizer has the general formula $R\text{-}(O\text{-}CH_2CH_2\text{-})_nOH$. R represents an aliphatic hydrocarbon radical with a maximum of eight carbon atoms and n represents a numeric value between 1 and 4. This general formula covers certain ethylene oxide condensation products of low molecular alcohols.

Preferred solubilizers or fixatives for direct dyes are 2-butoxyethanol 2-(beta-ethoxy)-ethoxy-ethanol, and the ethylene oxide condensation product of isobutyl alcohol. These compounds are applied in ratios ranging from five to 20 per cent of the dye solution.

An example calls for a solution of five per cent methyl isopicraminic acid, 20 per cent butyl "Cellosolve," three per cent triethanolamine, and water to make 100. This solution is applied for 15 to 20 minutes to hair which is 50 to 60 per cent grey. A good violet color will result.

Grey hair acquires a golden blond color by a 15 to 20 minute application of the following dye solution: one half per cent of 1-hydroxy-2-amino-5-nitrobenzene, 20 per cent butyl-"Cellosolve," three per cent triethanolamine, and water to make 100. This application must be followed by rinsing with water.

Multi-Purpose Cream Base

A highly versatile cream or ointment base is disclosed in Swiss patent No. 322,821. Suitable for shaving, hair, cleansing, skin, and sun creams, the base is composed of the following ingredients:

	parts
Cetyl stearyl alcohol	3
Fatty alcohol sulfonates	0.2-0.4
Water	70
Oleic acid oleyl ester	7-9
Oleum hyperici	2-3
Urea	1-2
Citric acid	0.2-0.4
Glycerine	3-5
Perfume	0.01-0.03

An oil-in-water emulsion is formed by the fatty alcohols to which oleic acid oleyl ester is added, as well as small amounts of fatty alcohol sulfonates, which act as emulsifiers. The ester endows the cream with detergent and foaming properties. Oleum hyperici and urea add hemostyptic and anti-inflammatory action; citric acid has astringent and disinfectant properties.

Lasting Gloss for the Hair

Good gloss is said to appear on the hair after it has been sprayed, brushed or rubbed with a solution containing the following:

	grams
Methyltriacetoxysilane	6
Dimethylsiliciumdiacetate	3
Tetra-ethoxytetra-methyltetra-siloxane	2
Methyl silicone (oil) visc. 13 cst.	4
Isopropyl alcohol	85

After the hair has been well dried it is thoroughly covered with the solution, set as desired, and then once more placed under the drier for five minutes at 45 to 50°C. Patent application by Wella A. G. Darmstadt, Germany.

Novel Cosmetic Cream

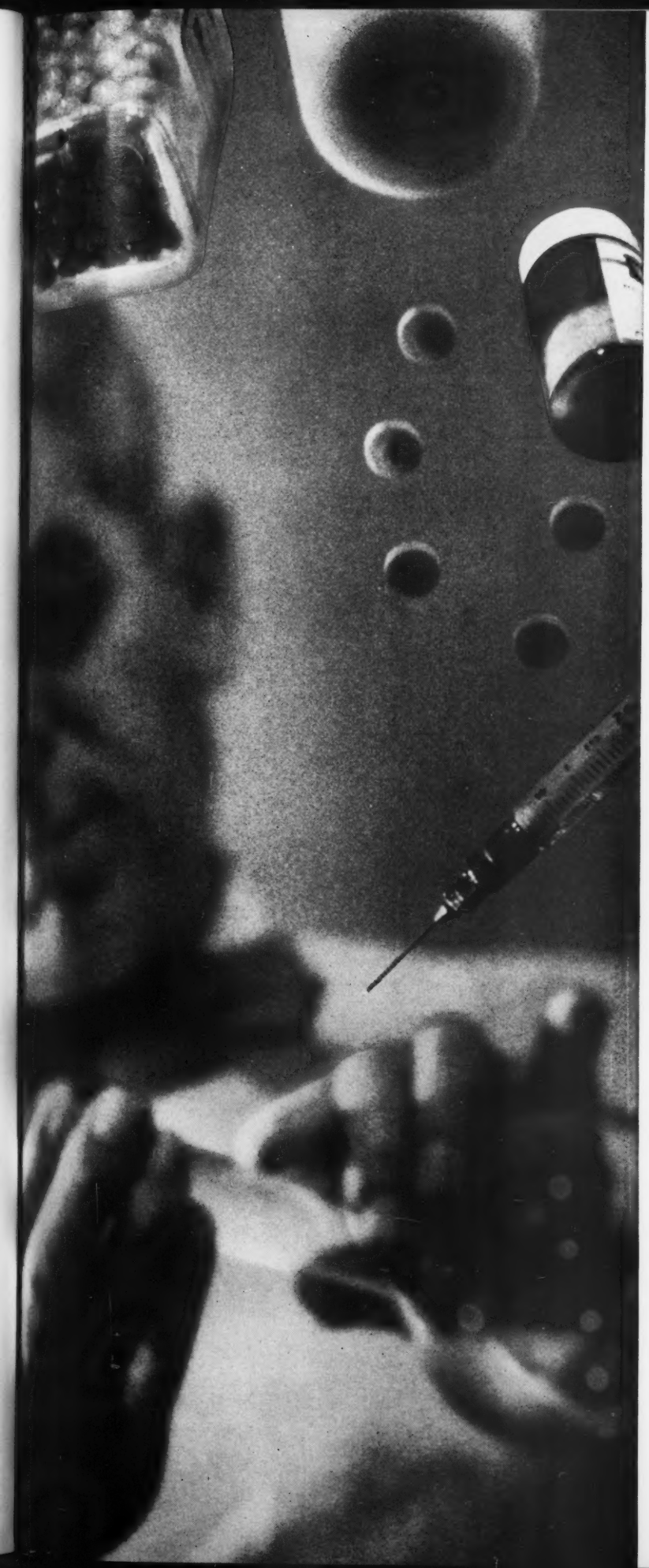
A cosmetic preparation of excellent clinging power contains (in addition to the usual ingredients) saturated polymer of an olefine having no more than four carbon atoms and a molecular weight exceeding 10,000 dissolved in a fatty acid ester having 10 to 12 carbon atoms and an alcohol having at least two to six carbon atoms. Such polymer/ester solutions are compatible with mineral oil derivatives; vegetable and animal fats, oils, and waxes, higher organic acids and alcohols; and with oil-soluble polysiloxanes. If no other than the above ingredients are present, the solution can be added directly to the mixture. Two examples of such formulations are supplied in Austrian patent No. 197,971.

Hair Cream

	per cent by weight
Petroleum jelly	77.5
Adeps lanae	20
20% solution of polyisobutylene in amyl oleate	2
Polysiloxane (oil) visc. 100 cst at 50°C	0.5

Skin Cream

Paraffine oil	14
Lanoline	24.5
20% solution of polyisobutylene in isopropyl stearate	0.5
Propyl-p-oxybenzic acid	0.1
Stearyl dimethyl-ethyl ammonium ethyl sulfate	0.01
Polyoxyethylene sorbitan monopalmitate	14.5
Water	46.3



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UNION CARBIDE CHEMICALS COMPANY

DIVISION OF UNION CARBIDE CORPORATION

Trade Literature

Perfume Catalog

Polak's Frutal Works, Middletown, New York, features impressionistic art on the 1959 catalogs. The first is the catalog of perfume bases, fixatives and specialties with a cover symbolizing a general feeling of perfume materials. Major emphasis is on the P.F.W. designation.

Packaging Machinery

The FMC Packaging Machinery Division, Stokes and Smith Plant, has available a new, four page folder describing the complete line of equipment. The literature covers, with illustrations, the eight product lines manufactured and sold by Stokes & Smith: Fillers, checkweighers, carton filling and sealing machines, casers, contour wrapping machines, box and tray forming equipment, wrapping machines and setup paper box machinery.

Aerosol Propellents

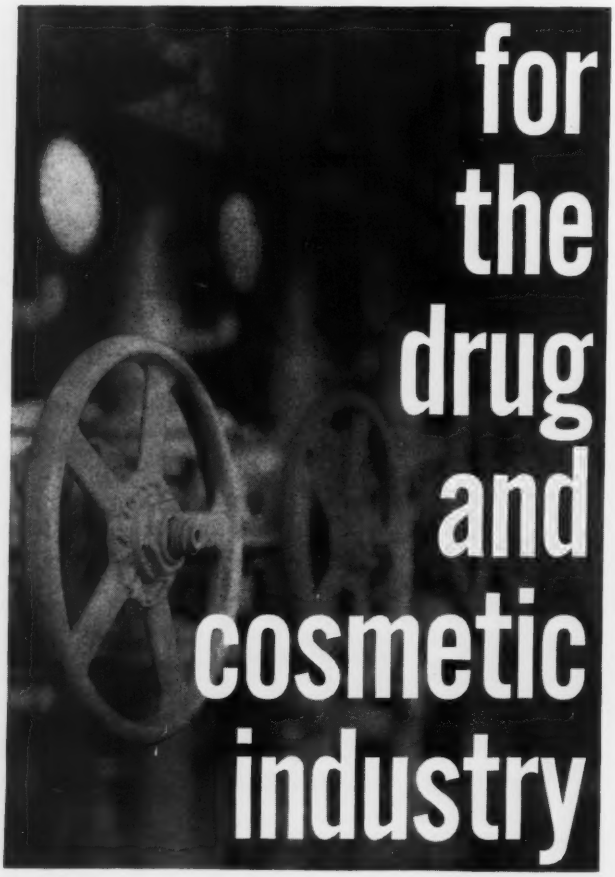
A new bulletin, with complete vapor pressure tables and other useful technical information on Isotron propellents has been published by the Isotron Department, Pennsalt Chemicals Corporation, 3 Penn Center, Philadelphia 2, Pa. The publication includes vapor pressure tables on mixtures of Isotrons 11 and 12 and mixtures of Isotrons 12 and 114 for temperatures ranging from −40°F. to 160°F.; and vapor pressure tables for 100 per cent Isotron 11, 12, 22, 113, and 114. A complete data report of the physical properties of the five propellants is also included in the new bulletin.

Industrial Filters

Comprehensive information about the new Corning Industrial Filters is given in a four-page bulletin just issued by Corning Glass Works, Corning, N. Y. The brochure covers product and property data in text, photographs and charts. The filters are designed primarily for filtration of corrosive fluids but also show promise in the fields of flow control, gas diffusion and purification.

Testing Services

The new six page bulletin 5801 describes the complete line of laboratory and field testing facilities and services available from United States Testing Company, Inc., Hoboken, N. J. These include engineering facilities and services, organic and inorganic chemical laboratory, materials testing, engineering inspection, scientific and commercial photography, textile labzoratory, package testing facilities, microbiology, microscopy, psychometrics and certification of product quality.



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Skin Research

Topical Triamcinolone Acetonide

In an effort to realize anti-inflammatory effect without sodium retention and edema, a new group of steroidal anti-inflammatory agents has recently been developed. One of the most potent members of this group, 9-alpha-fluoro-16-alpha, 17-alpha-isopropylidene dioxy-delta-1,4-pregnadiene - 11 - beta,21 - diol - 3, 20dione (which has the generic name of triamcinolone acetonide and referred to in this paper henceforth as *TA*), was shown to possess 40 times the anti-inflammatory activity of hydrocortisone in the adrenalectomized rat.

Double-blind studies were undertaken by F. W. Crowe, T. B. Fitzpatrick, S. A. Walker, R. Olson (*J. Invest. Dermatol.* 31: 297, 1958) to demonstrate the clinical usefulness of this preparation. Instead of a placebo control ordinarily used in this type of study, the manufacturer furnished the investigators with 1 per cent hydrocortisone lotion (referred to as *HC*), cream and ointment. The hydrocortisone preparation was identical in appearance and consistency with a preparation containing 0.1 per cent concentration of the TA.

Although the medication was provided in lotion, cream and ointment forms, patient acceptance was much better with the lotion and cream. The results with the lotion were more dramatic.

The results clearly define a greater anti-inflammatory effect when the TA is used. The subjective and objective changes on the side on which TA was applied have occurred in enough patients so that the sign test indicates significant differences between TA and HC which favor TA over HC at better than the 99 per cent confidence level.

A study of two patients applying 30 mg. of TA daily for seven days in a lotion form failed to demonstrate sodium retention or edema.

In a double-blind symmetrical paired comparison study, 0.1 per cent triamcinolone acetonide was compared with 1 per cent hydrocortisone topically in lotion, cream, by J. G. Smith, R. J. Zawisza, H. Blank (*A.M.A. Arch. Dermatol.* 78: 643, 1958) with 1 per cent hydrocortisone topically in lotion, cream, and ointment bases in a series of 109 patients. In this concentration triamcinolone acetonide was found to be a highly effective steroid and, in general, was superior to 1 per cent hydrocortisone. No effects suggestive of systemic absorption or toxicity were observed.

Embryonic Keratinization

Chemical and physical aspects of keratinization were studied by A. G. Matoltsy (*J. Invest. Dermatol.* 31: 343, 1958) in embryonic skin by histochemical and polarization optical methods. As an experimental material, the scalp of dated chick embryos was used.

The results indicate that sulfhydryl-rich proteins are not actively synthesized during the early phase of epidermal development. A thin layer, rich in sulfhydryl-containing protein is formed as early as the 10th day of embryonic life in the peripheral cytoplasm of the periderm cells but only on their exposed outer borders. This layer, which increases somewhat in thickness and persists up to about the 16th day of development, might represent an early protective layer for embryonic epidermis. A sulfhydryl-rich layer was also observed by Menefee in a corresponding region of the epidermis of 13-day mouse embryos, the earliest stage examined by Menefee. According to Menefee, this layer in the mouse consists of rows of small granules which are oriented parallel to the skin surface and appear to be associated with the cell wall.

The present study shows that true keratinization in the chick starts at about the 16th day of development. Intense production of —SH-rich protein and stabilization of keratin by —S—S—bonds takes place during the last few days of embryonic life. The cause of alterations in height of the epidermis during late epidermal development is not clear and cannot be explained on the basis of the present study. Hanson observed similar decrease in height of epidermis in both rat and mouse embryos at a late stage of epidermal development.

Topical Steroids and Rat Hair Growth

Seven analogs of hydrocortisone were compared by K. Fukuyama and B. L. Baker (*J. Invest. Dermatol.* 31: 327, 1958) with respect to their growth-inhibiting capacity, with local suppression of hair growth serving as the endpoint.

Finally, why does the hair-forming apparatus of the rat respond differently to adrenocortical steroids as compared with that of man? In the rat, systemic administration of corticotropin, the C-11 oxygenated steroids (hydrocortisone or cortisone) or the direct application of the latter to the skin inhibits growth of hair; conversely, adrenalectomy accelerates the rate at which hair grows. In man, treatment with excessive doses of C-11 oxygenated steroids may induce hirsutism while adrenocortical insufficiency may be accompanied by loss of pubic and axillary hair. Man and the rat may exhibit contrasting responses because of either a difference in responsiveness of the hair-forming tissue to the hormones or a difference in the *in vivo* catabolism of the steroids.

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U.S.I. CHEMICAL NEWS

Jan. ★ A Series for Chemists and Executives of the Solvents and Chemical Consuming Industries ★ 1959

Market for Rigid Urethane Foams Growing Rapidly

While rigid materials accounted for less than 10% of the total polyurethane foam market in 1957, 1958 figures are expected to show an increase to more than 20% of the total market. The Society of the Plastics Industry feels that by the end of 1959, 30-40% of the demand will be for the rigid foams.

The material is proving ideal for industrial and home insulation. Packaging applications are expanding. Makers of marine equipment are using the rigid foams for buoyancy. Military applications include radiation shields and heliohuts. More and more, structural panels and laminates are being made with rigid urethane foams.

Users can buy fabricated foam or they can foam the material themselves in place, by employing either molding or spraying techniques. Special equipment has been developed for spraying urethane polymer onto overhead, vertical or irregular surfaces. It foams and sets in place rapidly to give a rigid coat which will not slip, sag or fall away.

Rigid urethane polymers are formed by mixing two chemical components—polyisocyanates and polyesters. Carbon dioxide gas is given off during the reaction and it serves as a blowing agent which causes the polymer to foam in place. An intermediate that can be used to produce the polyester component is ISOSEBACIC® acid, a mixture of C-10 dibasic acids. ISOSEBACIC acid will be available soon in commercial quantities from a new U.S.I. plant at Tuscola, Illinois.

"Stabilized" Polyethylene Fabrics Now Being Made Via New Finishing Process

A patented technique for finishing polyethylene fabrics is now being employed to improve shrink resistance, strength, appearance and other physical characteristics. According to the patent, conventional finishing methods for polyethylene fabrics—calendering or hot fluid treatment of the greige goods to preshrink them—result in loss of yardage, strength and optimum appearance.

The patented process involves the pretreatment of oriented polyethylene filaments before conversion to give them a residual shrinkage of 8-20% (tested at 75°C for 20 minutes). The filaments are then converted to greige goods, in which they have a wavy form.

The greige goods are subsequently held along both the length and width to prevent retraction and are heated at a strictly controlled temperature for a limited time. So held and treated, the filaments in the fabric shrink to the extent of their residual shrinkage and straighten out, without reducing the area of the fabric.

By comparison with fabrics finished by conventional methods, these materials are said to have better appearance, strength and aging properties. The process is claimed to provide economies in operation — to save yardage and to reduce the number of finishing steps required.

Gov't. Authorizes Substitutions In SDA 40 Alcohol Formulation

Shortage of Brucine Denaturant Made Modifications Necessary.

SDA 40, which the U. S. Government authorizes for use in toilet goods, external pharmaceuticals, biocides, detergents, etc., has been formulated until now with ⅛ gallon of *tert.*-butyl alcohol plus 3 ounces of brucine alkaloid or 3 ounces of brucine sulfate per 100 gallons of ethyl alcohol. To relieve difficulties of denaturers and users of this formulation due to a critical shortage of brucine, the Internal Revenue Alcohol and Tobacco Tax Division (A. & T. T. D.) has authorized the formulation of SDA 40 with ⅛ gallon of *tert.*-butyl alcohol plus either 1½ ounces of brucine alkaloid, or 1½ ounces of brucine sulfate, or 1½ ounces of quassin per 100 gallons of ethyl alcohol.

How the Substitutions Came About

When the brucine shortage first became acute, an inability to meet customer requirements for SDA 40 threatened to upset the entire industry. Recognizing the situation, the A. & T. T. D. authorized quassin as an alternate denaturant.

While brucine is one of the bitterest materials known, quassin had been tested and found sufficiently bitter and acceptable from other standpoints to serve as an alternate denaturant. Quassin had been used as a denaturant in Canada for 25 years, and this experience dispelled concern about possible adverse effects arising from its use.

Samples of SDA 40 denatured with quassin were offered to the trade, and users were urged to make up their products with this alternate, to assure compatibility with their formulas. After testing, many customers advised that they would accept SDA 40 alcohol with this denaturant.

However, realizing that limitations on the supply of quassin made it an incomplete answer to the shortage, the A. & T. T. D. took quick action to extend existing supplies of brucine by authorizing denaturation with reduced quantities of brucine alkaloid and

MORE

SDA 40 AUTHORIZED USES
(Under Permit)

- Hair and Scalp Preparations
- Bay Rum
- Lotions and Creams (Hand, Face, Body)
- Deodorants (Body)
- Perfumes and Perfume Tinctures
- Toilet Water and Colognes
- Shampoos
- Soaps and Bath Preparations
- External Pharmaceuticals (not U.S.P. or N.F.)
- Disinfectants, Insecticides, Fungicides and Other Biocides
- Cleaning Solutions (including Household Detergents)
- Theater Sprays, Incense and Room Deodorants
- Miscellaneous Dye Solutions
- Miscellaneous Solutions

Vitamin C Indicated for Virus & Other Infections

Several medical investigators have found that continuous massive doses of ascorbic acid (Vitamin C) are effective in treating virus diseases such as polyiomyelitis, measles and virus pneumonia; bacterial infections such as tuberculosis and scarlet fever; and cases of poisoning such as snake bite and lead poisoning. The range of antibiotic and antitoxic action is said to be unusually broad, and, in addition, there is claimed to be *complete freedom from allergic or toxic reaction.*

Intravenous or intramuscular injection is the preferred method of treatment. When so administered, ascorbic acid is said to compare favorably with sulfa drugs and mycelial antibiotics. Effectiveness of the therapy is reported to be dependent upon the potent oxidation-reduction action of ascorbic acid, which rapidly neutralizes viral or bacterial toxins.

Ascorbic acid occurs naturally in citrus and other fruits, as well as green leafy vegetables. One method of producing it synthetically is by using L-sorbose as the starting compound and employing *sodium methoxide* in the final (enolization) step of the synthesis.

Index of Chemical Patents Now Being Prepared

Every patent relating to chemistry which has been issued by the U. S. Patent Office since 1950 is being collected and indexed for reference purposes by a Washington information service. The collection is being kept current and is being made available on a subscription basis to chemical companies, libraries, educational institutions and other interested organizations.

At the moment, indices for 1955, 1956, 1957 and the first 10 months of 1958 are available. They cover 30,000 patents. A trained staff of chemists and biochemists is now working on the indices for 1950-1954, which will add another 40,000 patents. It is estimated that when this work is completed, in about two and one-half years, more than 100,000 patents will have been collected and indexed.

It is claimed that the indexing method used analyzes, edits, classifies and cross-indexes U. S. chemical patents into the fastest and most accessible reference system ever devised.

CONTINUED *Alcohol*

brucine sulfate. Consequently, there are now three new SDA 40 formulations approved by the Alcohol and Tobacco Tax Division. U.S.I. designations are shown in the box below.

U.S.I. Designations for New SDA 40 Formulas

SD-40-1M .....1½ oz. brucine alkaloid
SD-40-2M .....1½ oz. brucine sulfate
SD-40-3 .....1½ oz. quassin

U.S.I. Studying Alternate Denaturants

Because brucine and quassin derive from natural imported products, there is always the possibility that the supply of these denaturants might be inadequate at some future date. U.S.I.'s research laboratories are therefore continuing studies to develop suitable additional alternates.

Ideally, alternate materials suitable as denaturants should be synthetic and domestically produced. Once found and tested in end-use formulations, such stand-by alternates—pending approval by the government—would assure denatured alcohol consumers of an uninterrupted flow of raw material at all times.

Methionine-Hormone Formulation Effective For Treating Acne

Clinical studies have revealed that a formulation of DL-acetyl methionine, estrogenic hormone, colloidal sulfur and resorcin applied to the skin is effective for treating acne conditions.

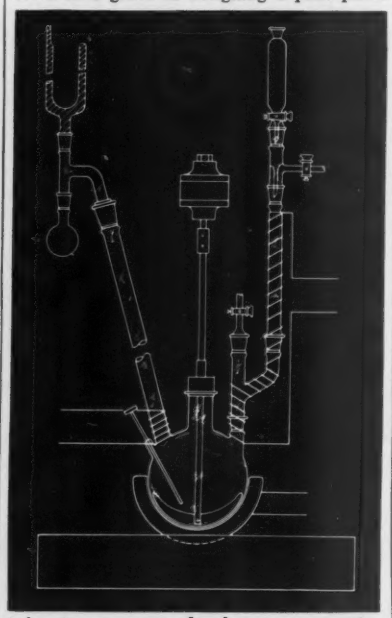
The medical research workers who conducted these studies found that methionine—the sulfur-bearing amino acid—and the estrogenic hormone act synergistically to reduce the excessive secretion of fatty materials from the sebaceous glands—a characteristic condition in acne cases. Consequently, the formulation dries and heals the acne lesions rapidly.

For optimum results, the treatment was supplemented with dietary and hygienic routines, and small oral doses of thyroid extract and estrogenic hormone.

Pure Sodium Alkoxides Can Be Made by Dry-Way Process

A new technical bulletin just released by U.S.I. describes a valuable but little-known technique for preparing sodium alkoxides from metallic sodium and alcohol vapors. This low-cost, dry-way process yields powders which are high-analysis alkoxide, in contrast to the 16-18% alkoxide solutions produced by the usual method of introducing sodium into liquid alcohols. It provides a way for pharmaceutical and other manufacturers who make their own alkoxides to get a high-purity material.

Products are almost identical in analysis to commercially available alkoxides. Although the bulletin describes the laboratory technique of passing vaporized alcohols over molten sodium, sufficient data is available to serve as a guide in designing a pilot plant.



Laboratory apparatus for dry-way preparation of sodium alkoxides.

TECHNICAL DEVELOPMENTS

Information about manufacturers of these items may be obtained by writing U.S.I.

L-Methionine, labeled with both carbon-14 and deuterium (methyl-$C^{14}D_3$), can now be obtained for research purposes. This amino acid is reported useful in studying the mechanism of ergosterol. **No. 1430**

Cosmetic technology is discussed in new, 1450-page book now being sold. In 53 chapters, 61 experts cover over 3 dozen types of products. Includes technology, historic and legal aspects, physiology, testing, manufacture. **No. 1431**

Slide rule for chemists has special scales for solving pressure, temperature, solution concentration problems on one face, standard scales on other face. Gives atomic wts. of 52 elements, molecular wts. of 18 atomic groups. **No. 1432**

Chloromethoxypropyl mercuric acetate solutions now available in commercial quantity. Fungicidal and bactericidal activity claimed superior to phenyl mercuric compounds, due partly to presence of labile chlorine atom. **No. 1433**

Uses of stainless steel in CPI discussed in newly revised, 40-page free booklet. Sections on fields of plastics, detergents, nuclear power, others. Includes corrosion resistance table and table comparing stainless grades. **No. 1434**

Full line of polyesters for producing rigid or flexible urethane foams can now be obtained commercially. For rigid products, combinations of prepolymer and polyester are offered for foaming in place by mixing or spraying. **No. 1435**

Long-path infrared system recently developed is said to detect evaporation from one drop of a predetermined chemical in an average room. System senses the chemical by its IR spectrum, is not usually sensitive to other materials. **No. 1436**

Polyethylene work gloves now on market are claimed to provide protection without loss of fingertip sensitivity. Are lightweight, waterproof, resistant to most chemicals. Said to be suitable for use with radioactive materials. **No. 1437**

Comprehensive file of trademarks used by CPI here and abroad is now available for reference at a charge. Includes registered, unregistered, common, scientific, technological names. Composition, uses, producer given in many cases. **No. 1438**

New analytical-grade ion-exchange resins based on cellulose are claimed suitable for chromatographic fractionations of high-molecular-weight materials beyond range of conventional resins. Are extremely porous and hydrophilic. **No. 1439**

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Proprietary Denatured Alcohol Solvents: SOLOX® — General-purpose. FILMEX® — Special, authorized for certain industries. ANSOL® M — Anhydrous, special blend for lacquers, resins, etc. ANSOL® PR—Anhydrous, special blend with higher ester content and solvency for lacquers, resins, etc.

OTHER PRODUCTS

Organic Solvents and Intermediates: Normal Butyl Alcohol, Amyl Alcohol, Fusel Oil, Ethyl Acetate, Normal Butyl Acetate, Diethyl Carbonate, DIATOL®, Diethyl Oxalate, Ethyl Ether, Acetone, Acetoacetanilide, Acetoacet-Ortho-Chloranilide, Acetoacet-Ortho-Toluidide, Ethyl Acetoacetate, Ethyl Benzoylacetate, Ethyl Chloroformate, Ethylene, Ethyl Sodium Oxalacetate, Sodium Ethylate, ISOSEBACIC® Acid, Sebacic Acid, Urethan U.S.P. (Ethyl Carbamate), Riboflavin U.S.P., Pelargonic Acid, 2-Ethyl Heptanoic Acid.

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Animal Feed Products: Antibiotic Feed Supplements, BHT Products (Antioxidant), Calcium Pantothenate, Choline Chloride, CURBAY B-G®, Special Liquid CURBAY, VACATONE®, Menadione (Vitamin K_3), DL-Methionine, MOREA® Premix, Niacin USP, Riboflavin Products, Special Mixes, U.S.I. Permadry, Vitamin B_{12} Feed Supplements, Vitamin D_3, Vitamin E Products, Vitamin E and BHT Products.

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(*Continued from page 59*)

ACTH in saline." This argument was based on an affidavit of Thompson, dated May 29, 1952, which contained the results of a rat test ostensibly comparing ACTH in gelatin with ACTH in saline.

(33) The Thompson affidavit was refiled in the continuation-in-part application and the conclusions of the affidavit were set forth in the specification of the continuation-in-part application, and, eventually, in the patent. The patent as issued asserts that ACTH-gelatin preparations produce "immediately upon injection, a sudden strong response which is substantially in excess of the response caused by an equal dose of the same substance in an aqueous solution from which the gelatin is omitted."

The patent also asserts that gelatin-ACTH gives a response which is always stronger at any point of time than an equivalent dosage of saline-ACTH, and this is based on a "unique property of the gelatin which is displayed when the gelatin is used in combination with the adrenocorticotrophic hormone." This alleged "unique" property of gelatin is also referred to as "potentiation" (Patent, column 2, lines 14-38).

(34) These assertions were based on a single test in rats.

(35) Wilson conducted numerous rat tests, including an inter partes test. The Wilson tests employed many rats and compared all four vehicles; the result is always the same—both saline plus phenol and gelatin plus phenol show a greater response than the two vehicles without phenol.

(36) Contrary to the statement made to the Patent Office in Thompson's affidavit that his rat test compared ACTH in gelatin with ACTH in saline, the test actually compared ACTH in a gelatin-phenol vehicle with ACTH in a saline vehicle without phenol.

(37) Thompson's misleading affidavit was filed despite the fact that he had been earlier advised by Dr. Forsham that phenol had an effect.

(38) The only rat test produced by Thompson comparing all four vehicles (saline, gelatin, saline plus phenol, and gelatin plus phenol) was assay 68 performed in 1955; this single Armour test shows, just as the many Wilson tests do, that saline with phenol produces an equivalent response to gelatin with phenol.

(39) Plaintiff introduced recently made clinical tests during the course of the trial, but the earliest determinations made in these tests were after eight hours, except for Dr. Frawley's four-hour eosinophil test, which showed other vehicles to be more effective than gelatin and which were asserted by plaintiff not to be a useful index of ACTH activity. The evidence with respect to humans establishes from plaintiff's own witness, Frawley, that with ACTH in gelatin, the effect does not appear quite as suddenly, but does appear to last longer than with ACTH in saline; Thompson refused to state whether or not he agreed with this evidence. Thompson was an evasive and equivocating witness.

(40) Thompson's assertion in his patent that gelatin is "unique" and exerts a "sudden strong response" was based on the single affidavit test in rats and this single test was false and misleading.

VII. *Improper prosecution of the Thompson application—gelatin vs. PVP.*

(41) When Thompson filed his continuation-in-part application in December, 1952, he made a new assertion, not found in his original application, that there was a difference between gelatin on one hand and "retarding agents" on the other hand, one of such "retarding agents" being PVP (patent, column 4, lines 43-65.)

(42) When Thompson first told the Patent Office that there was a difference between gelatin and PVP, he well knew the statement was false, inded he had conducted an experiment comparing the effect of ACTH with gelatin and ACTH with PVP and determined that PVP acted in the same manner as gelatin.

(43) In application serial number 352,290, which Thompson filed on the combination of ACTH and PVP (see finding 30, above) he asserted that PVP gave a sudden strong response that is prolonged for a doubly extended period; this is essentially the same assertion that Thompson made with respect to the action of gelatin in attempting to convince the Patent Office that gelatin was "unique" and differed from "retarding agents" such as PVP.

(44) Thompson furnished false and misleading information to the Patent Office, knowing it to be false and misleading, when he asserted in his continuation-in-part application and, ultimately, in his patent that gelatin was "unique" in its action and different from "retarding agents" such as PVP.

Conclusions of Law-Thompson Patent

(1) The claims of the Thompson patent are invalid because the use of gelatin with ACTH was obvious (common sense) to those skilled in the art.

(2) The use of gelatin with ACTH is merely an analogous use for gelatin, a substance well-known to increase the effectiveness of drugs, and such use of gelatin does not amount to invention.

(3) The claims of the Thompson patent are invalid for lack of invention over the prior art.

(4) Even if it be assumed that gelatin was discovered by Thompson to possess characteristics in addition to its well-known retarding characteristics, the discovery that gelatin possessed these characteristics does not amount to invention, inasmuch as gelatin was long known to increase the effectiveness of other drugs and would be expected to increase the effectiveness of ACTH. The discovery of a function is not patentable.

(*Continued on page 123*)

(*Continued from page 27*)

seemed abstruse and academic has come to be of immediate practical interest.

To produce the great quantities of fuels needed to drive society's motors, scientists have devised very ingenious methods and huge equipment. But in developing catalytic manufacture of energy—releasing compounds men were only learning to do, consciously, with inorganic materials something similar to what very low forms of life were doing in their one-celled bodies millions of years before man appeared on earth, and what all forms of life have been doing ever since then.

All living cells, as Tauber[3] points out, can and must produce and utilize catalysts, and no cell can live without them. These catalysts, which protoplasm makes and uses, are called enzymes; they are the agents that supply all living things with the energy required for work and for biosynthesis, in other words, for life and growth. Thus Tauber feels that we may say, "Life is a series of catalytic reactions controlled by genes."[3]

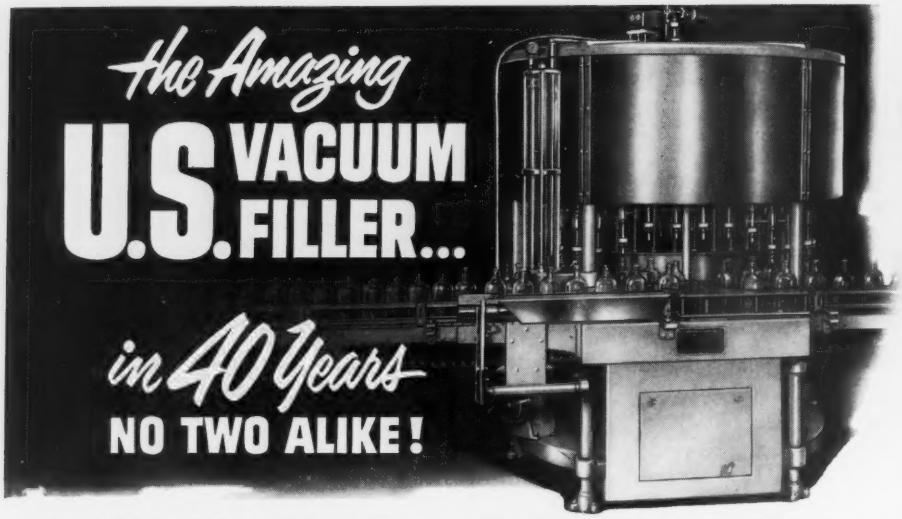
It is not easy to formulate an acceptable definition of the word "enzyme," and modern knowledge has made old definitions inaccurate. The word was coined from Greek roots (*en* meaning in and *zyme*, meaning leaven) by W. Kuhne in 1878.

If we look into the nature of enzymes, we learn first that they are biochemical catalysts. Typically, catalysts are substances which cause or accelerate chemical reactions between other substances without themselves being changed in the process. Inorganic catalysts may often be recovered unchanged and in undiminished amounts after they have catalyzed reactions. This is not true of most biochemical catalysts, however, for they are commonly partly inactivated in catalyzing the reaction.

Genes, hormones, and viruses are also biochemical catalysts, but are not enzymes. Although adenylic acid, ascorbic acid, cytochrome, and glutathione take part in various enzyme reactions, they are not enzymes; they undergo ordinary chemical changes, such as oxidation and reduction.

In chemical composition all enzymes are protein, either entirely or in part. Such well-known enzymes as pepsin and trypsin consists of protein only. Certain other enzymes, such as carbonic anhydrase, are made up of a protein component and a cation (magnesium, copper, etc.). In some cases the enzyme molecule contains a protein and a nonprotein coenzyme or prosthetic group; and in still other cases the molecule also contains a cation in addition to these two components.

An important and most striking characteristic of enzymes is their specificity in action. Tauber[3] emphasizes this fact and points out this difference from inorganic catalysts, which may catalyze many reactions. For example, hydrogen ions will hydrolyze pro-



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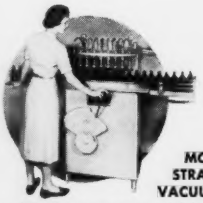

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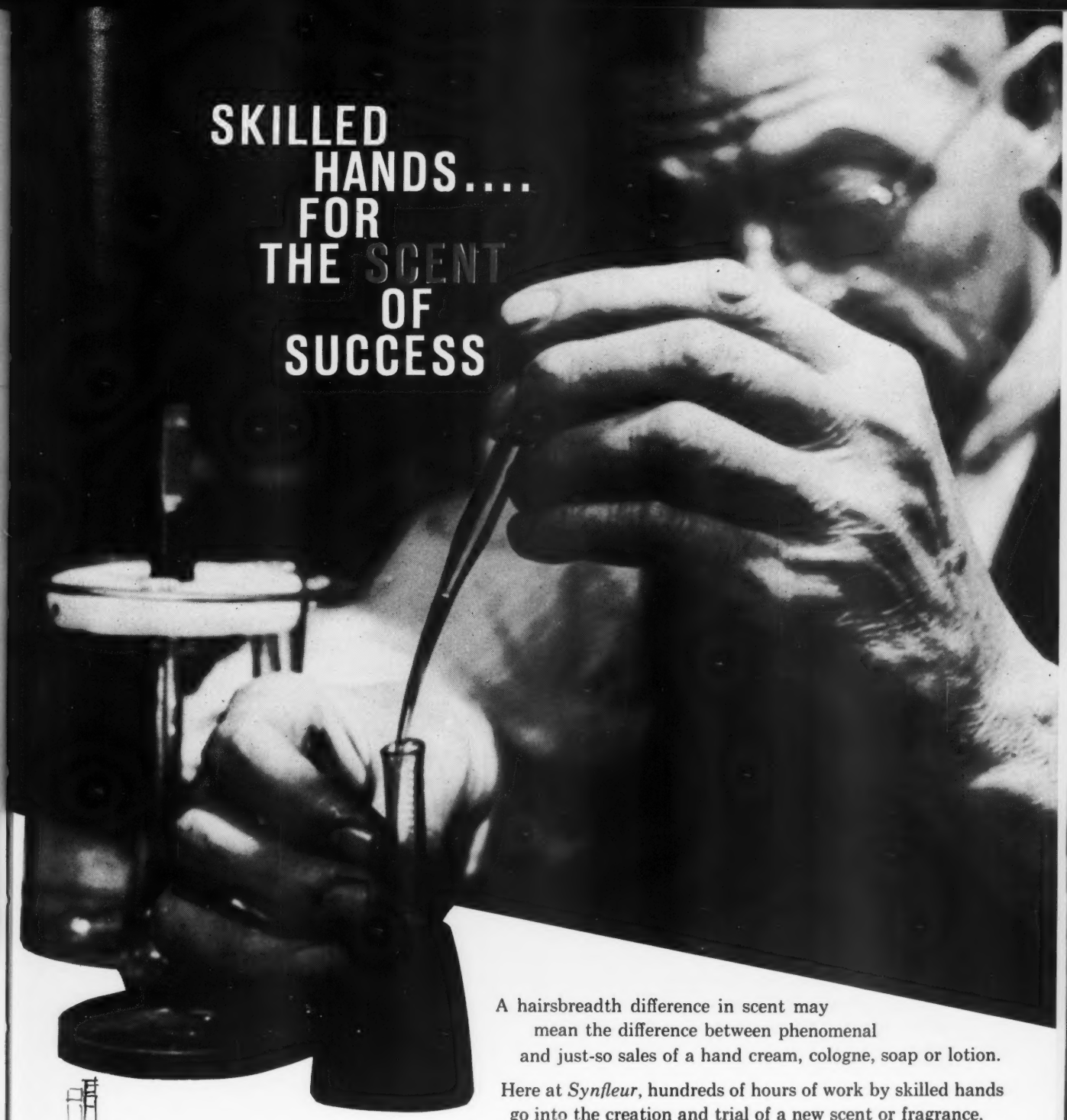

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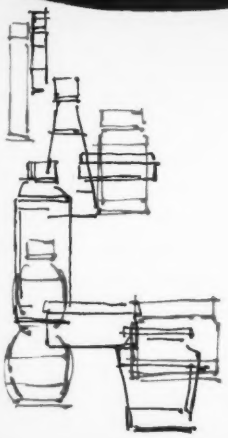

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teins, fats, carbohydrates, and any ester; and hydroxyl ions perform in a similar manner. But lipases do not split proteins, and proteases do not attack fats. The degree of specificity extends even to a distinction betwen isomers, or between different molecular linkages. Certain enzymes act on a variety of compounds but may still be specific in the end products produced from certain substrates. With these same substrates other enzymes catalyze different reactions, resulting in different end products.

Dixon and Webb[4] say that the high specificity of enzymes is one of the most important biological phenomena, without which the ordered metabolism of living matter would not exist and life itself would be impossible. Hopkins[5] said in 1932, "It is at any rate sure that the inter-related activity of highly specific catalysts represents a notable device of nature which has supported during the course of evolution those dynamic manifestations which characterize living things."

Although enzymes are produced only by living cells they can act independently of the parent cells. Another characteristic of enzymes is that they are relatively heat labile. Tauber[3] says that above 50° C. enzymes in solution are rapidly inactivated, and that with most enzymes destruction is complete at 80° C. Thus, we might define "enzyme" as a specific, cell-independent, heat-labile, biochemical catalyst.

Many enzymatic reactions require a "cooperative partner" called a coenzyme. Hunnekens[6] says that the coenzyme has also been called "cofactor," "prosethetic group," or "activator." He says it is usually a heat stable, dialyzable, organic molecule or metal ion. In rare cases a simple anion (Cl^- with amylase) serves as coenzyme. Since almost all coenzymes contain a nitrogenous base (often a vitamin), a sugar (ribose) and a phosphate group, these substances are in the class of compounds called nucleotides. Incidentally, an enzyme free of its co-enzyme is called the apoenzyme.

We can see, then, that man has inherited essential metabolic equipment from his remotest ancestors. Likewise, unknown to him other enzymes have served him well since the beginnings of civilization, and have eventually led him to explore this enormous field of vital knowledge.

The phenomenon of digestion had been observed and studied by Beaumont for several years when, in 1833, Payen and Persoz found that an alcohol precipitate of malt extract contained a thermolabile substance which converted starch into sugar. They called this substance "diastase" because of its power to separate soluble dextrin from the insoluble envelopes of the starch grains. Dixon and Webb[4] say this was probably the first clear recognition of an enzyme. The word diastase later came to be used as a general term for enzymes. Duclaux proposed the use of "ase" as a suffix to be attached to a root indicating the nature of the substance on which the enzyme acts, and this provided a basis for systematic nomenclature.

Although Pasteur pioneered in the microbiology of fermentation, Tauber[3] says Buchner was the first to prove that the living cell is not necessary for enzyme action.

Dixon and Webb[4] say the beginnings of enzymology can be traced back to the early nineteenth century, but these and other authors stress the fact that enzymology is a relatively new science. Its great developments have come during the last 35 years. According to Hunnekens,[6] since 1920 the field of enzyme chemistry has evolved from a tiny island in the realm of biochemistry to such vast proportions that it begins to overwhelm the field by virtue of its almost universal applicability. Illustrating the "accelerated pace in enzymology," he says it took a number of years in the 1930's for Warburg to complete his classical studies showing that the oxidation of glucose-6-phosphate was mediated by the concerted action of four highly purified components—two proteins, a dehydrogenase, and an electron carrier—and two coenzymes. Today, he says, isolation and description of a new enzyme system, perhaps with its attendant coenzyme, is greeted with far less amazement, simply because such events have become commonplace. "Each plateau of knowledge . . . becomes . . . a stepping stone to the next higher level."

According to Dixon and Webb[4] the serious purification of enzymes did not begin until about 1920. Next came the preparation of an enzyme in crystalline form, the first one being urease obtained by Sumner in 1926. It was far from pure but it was a start. Even 20 years ago the number of purified enzymes was very small. Now the number in pure and crystalline form approaches 100, and more than 500 have been more or less purified. It is of interest that all the enzymes that have been isolated in the pure state are proteins.

In the early days of enzymology the principal interest was centered in the enzymes of digestion and fermentation; only much later was the importance of the intracellular enzymes recognized. "In fact the serious purification of *intracellular* enzymes did not begin until 1937, despite the fact that comparatively few enzymes occur naturally outside living cells. Since that date the emphasis has entirely changed, and the enormous increase in the number of known enzymes has been largely due to the discovery of new intracellular enzymes. . . . Photosynthesis, respiration and biological oxidations, fermentations, the synthesis of many organic compounds required for growth, the performance of mechanical or osmotic work, are among the processes on which a flood of light has been thrown by the isolation and study of the enzymes responsible."[4]

Some idea of the great progress which has been made in enzymology, and of the magnitude and im-

(*Continued on page 106*)

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An Introduction To The Chemistry Of Fats And Fatty Acids, *by F. D. Gunstone, Ph.D., Lecturer in Chemistry, The University of St. Andrews, 161 pp., John Wiley & Sons Inc., New York, (1958), cloth,* **$6.**

The first chapter of this work is given to a discussion of the fatty acids as the most important structural units of the fats, and is followed by an account of the chemical nature of the latter. Following a short chapter dealing with physical properties, there is a longer report of the chemical properties of fats and their component acids. Finally, there are two short chapters on some biochemical and technical aspects of the subject. Contents: Chapter 1, The Fatty Acids; 2, The Chemical Nature of Fats; 3, The Physical Properties of Fats and Fatty Acids; 4, The Chemical Properties of Fats and Fatty Acids; 5, The Synthesis and Utilization of Fats in Living Organisms; 6, The Chief Technical Applications of Fats.

The following paper-bound books were recently published by the American Management Association, Inc., New York, N. Y.

Establishing A New-Product Program (Guides for Effective Planning and Organization. *Report No. 8—124 pp., (March 1958)* **$3.00** *(AMA members* **$2.00**).

Operations Research Reconsidered (Some Frontiers and Boundaries of Industrial OR). *Report No. 10—143 pp., (May 1958)* **$3.75** *(AMA members* **$2.50**).

The District Sales Manager (His Problems, Practices and Responsibilities). *Report No. 11—98 pp., (June 1958)* **$3.00** *(AMA members* **$2.00**).

Plastic Sheet Forming (Materials and Methods for Packaging and Industry). *Report No. 12—139 pp., (June 1958)* **$3.75** *(AMA members* **$2.50**).

How To Plan Products That Sell (Guides for Development and Commercialization). *Report No. 13—147 pp., (July 1958)* **$3.75** *(AMA members* **$2.50**).

Flavor Research And Food Acceptance, *Sponsored by Arthur D. Little, Inc., Published by Reinhold Publishing Corp., New York, 391 pp., (1958), cloth,* **$10.**

Based on a series of four symposia, this book integrates the various facets of the subject and presents them in perspective. These facets include: (1) what physiologists and psychologists have found out about the bases and importance of taste and smell; (2) what chemists know of the chemical aspects of flavor; (3) what market research knows of consumer wants; and (4) what methods are used in sensory flavor analysis. The chapters are by a large group of acknowledged leaders in the field who represent many diverse industries including food, beverage, confection, essential oils, petroleum, market research and research consulting companies. In addition to the industries represented by chapter authors, cosmetic, pharmaceutical, advertising, chemical and packaging companies rendered key assistance in planning the presentation.

A Bibliography Of Internal Medicine (Communicable Diseases) *by Arthur L. Bloomfield, M.D., 560 pp., The University of Chicago Press, (1958), cloth,* **$10.**

The surge of new knowledge in medicine has created a tremendous problem . . . The student tends to keep up on the new, the curious, and the esoteric at the expense of the fundamental and the historical. In current medical writing what is referred to as the "older literature" often turns out to be that of the previous decade . . . In brief, there is a real danger that we shall become completely cut off from our medical past and relapse into a sort of modern Dark Age.—From The Preface. To help obviate this very real danger, Dr. Bloomfield has compiled a definitive and exhaustive bibliography of communicable diseases with substantial excerpts from practically every important reference made to each of thirty such diseases from 1800 on.

Schizophrenia, *by Manfred Sakel, M.D., 335 pp., Philosophical Library, New York, (1958), cloth,* **$5.00.**

Sakel Insulin Therapy not only revolutionized medicine's whole attitude toward endogenic psychoses, but has given new life and hope to thousands of mental patients and their families throughout the world. Here is Dr. Sakel's own personal account of his epoch-making discovery, its clinical operation and its consequences for psychotherapy. Part I investigates the "theoretical" background: the history and description of schizophrenia—the doctors and scientists who contributed to this new branch of medicine—causes and classifications of the illness, symptoms, diagnosis and prognosis. Part II is devoted to Sakel's own clinical description of his treatment, with full medical data and detailed records of many case histories.

The Encyclopedia of Chemistry (Supplement), *George L. Clark, Research Professor, University of Illinois, Editor-in-Chief, 330 pp., Reinhold Publishing Corp., New York, (1958), cloth,* **$10.**

The Supplement adds over 200 concise articles of primary and current importance to the Encyclopedia of Chemistry. The arrangement of the Supplement is identical to that of the parent book; articles appear alphabetically by subject. Each article is written by a respected authority in science and/or industry. A wealth of information is contained here for those who seek to understand current scientific events by referring to such topics as antidotes, porphyrins, barbiturates, plasma, chemical education, propellants, cermets, dosimetry, fluoridation, resonance and scores of others.

Increasing Pharmacy Profits *by Frank T. James, 148 pp., J. B. Lippincott Co., Phila., (1958), cloth,* **$4.75.**

Among other important suggestions, economical ways of handling store operations are discussed here. For example, controlling inventory, pricing, buying, accounting and dispensing. Also, many specific sales suggestions covering layout, display, training, professional relations, self-service and premium programs are included.

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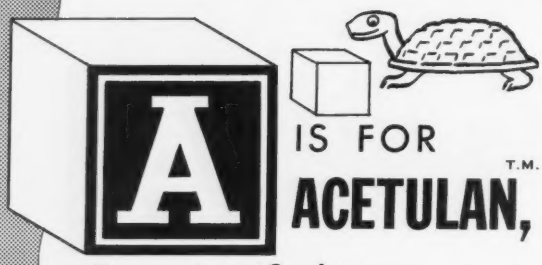

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AMERCHOL PARK — EDISON, N. J.

(*Continued from page 102*)

portance of enzyme functions can be obtained by merely looking over the table of enzymes presented by Dixon and Webb in their superb new book *Enzymes*. Beginning with such old friends as pepsin, trypsin, thrombin, and papain, we find no less than 221 "hydrolyzing enzymes" listed, together with their substrates or reactions.

"Transferring enzymes" number 359, and 182 of them transfer hydrogen alone. Grouped as "other enzymes" are 24 that catalyze synthetic reactions linked with breakdown at ATP (adenosine triphosphate) or GTP (guanosine triphosphate, and 39 that add groups to double bonds. Hydrolysis can be regarded as a transfer of one part of the substrate molecule from the other part to a hydroxyl from water; thus over 90 per cent of enzyme reactions are transfer reactions. And, despite the great multiplicity of enzymes, "from the point of view of reaction types the picture is one of comparative simplicity." The table comprises 659 enzymes and was believed to be a complete list of those known at the time of publication in 1958.

Where is enzymology going? All the most eminent students of the subject foresee its continued expansion to still greater domination of biochemistry.

Efraim Racker[7] says, "Enzymes as analytical tools will undoubtedly infiltrate further into the laboratories at the extreme wings of biochemistry, physical chemistry and medical diagnostics. Many more enzymes will be investigated as reactants, and cycle after cycle will appear on the surface of the deep waters of metabolism."

According to Pauling:[8] "The problem of enzymes encompasses essentially the whole of biology. When we understand enzymes—their structure, the mechanism of their synthesis, the mechanism of their action—we shall understand life, except for those aspects of life that involve mental processes; and I have no doubt that enzymes are important for these too.

"Enzymology as a science now stands where organic chemistry stood a century ago, before the structural formulas of chemistry were developed. . . . The time is rapidly approaching where enzyme chemists will use structural formulas of activated complexes, and structural formulas of the enzymes with all interatomic dimensions correct; when this time comes, enzymology will have reached the stage in its development that has now been reached by organic chemistry."

In the preface to *Currents in Biochemical Research*, David E. Green writes: "A direct consequence of the advances in methodology was the growth of enzyme chemistry from a toddler to a giant dominating the whole of biochemistry. During the past ten years practically all the enzymatic and chemical details of the citric, pentose, fatty acid, and urea cycles have been elucidated. Then enzymatic synthesis of nucleic acid, lecithin, cephalin, fatty

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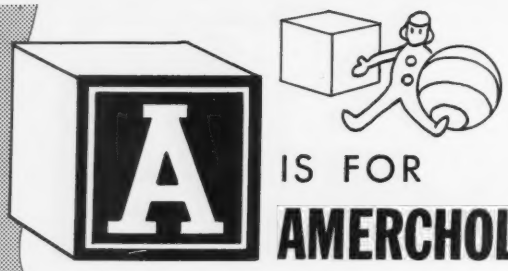

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AMERCHOL PARK — EDISON, N. J.

(*Continued from page 106*)

acids, sucrose, lactose, purines, pyrimidines, and dinucleotides has been accomplished by means of isolated enzymes or cell-free enzyme systems. . . . The list of coenzymes has more than doubled during the past ten years. . . . A whole new industry has sprung up which provides practically every important biochemical compound relatively inexpensively and of high purity.

A few companies have been devoting extensive facilities and large, highly competent technical staffs to the manufacture of enzyme products and the advancement of enzymic technology for many years. These companies, Wallerstein Company, for example, have rendered invaluable service to such diverse industries as brewing, baking, textile, and leather processing. They have also served the pharmaceutical industry by producing pure standardized enzymes. Now, with technologic advances being made with increasing frequency, the enzyme makers bring their facilities and their know-how to the pharmaceutical manufacturer.

The enzyme manufacturer stands ready to deliver products of immediate utility and to deliver others for future use. The present resources are greater than is commonly realized. For example, a patient allergic to digestive enzymes of animal origin was recently treated with complete satisfaction by means of enzymes of vegetable origin. The enzymes of plants, bacteria and fungi provide a very substantial resource from which to develop new products, some of enzymic activity alone, others having such activity combined with that of other therapeutic agents.

The use of proteolytic enzymes to prevent or relieve strokes and coronary thrombosis has already been commented on. There is, moreover, the use of mucolytic preparations to treat chronic lung conditions—emphysema, chronic bronchitis, bronchiectasis, and cystic fibrosis. The same mucolytic action may find routine application in gynecology, both for office treatment and personal hygeine. And how about stepping up the potency of digestive products by addition of cellulases to break down undigested vegetable fibres? Use of this type of product in geriatric practice is already under way in Europe and may soon become common in the United States.

Still another promising therapeutic field is the use of enzyme inhibitors to modify abnormal metabolic processes. This has already been undertaken. An example of such studies appears in a symposium on amine oxidase inhibitors, recently held at the New York Academy of Sciences, New York City.

Being at the strategic intersection of biophysics and biochemistry, enzymology plays a role of importance in physiology (normal function) and pathology (disturbed function); moreover it can play such a role in therapeutics (the attempt to re-establish normal function). Thus, this science has an obvious ap-

(*Continued on page 110*)

(*Continued from page 43*)

study the X rays, the blood count and the basal metabolism report, can he feel that he is on perfectly safe ground. Then his work becomes one of real creative effort. But he must constantly refer to information he has gathered as a check-list. For, while a package can be beautifully designed, it cannot succeed, unless all of the problems that confront it have been considered, when it finally gets onto the shelf.

At this point I might pause a moment to dispel myth number one, in regard to the package designer. He has a reputation for fabulous fees. Some of this is a result of poor publicity and, of course, poor judgment on the designer's part, but most of it is a result of people's not understanding the careful step-by-step operations that I have described which must go into a successful package. As a matter of fact, the package designer seldom gets enough for his efforts. While the total responsibility of a successful package rests in his lap, his fee may not equal the cost of the full-color plates to reproduce the package for its first run!

After the package designer has designed what he believes to be the best solution to the problem, how does he know he is right? The answer, of course, is simple. Nobody really knows for sure whether he is right or wrong until his efforts have been tested on the shelf under normal shopping conditions—and the shopper either picks it up or rejects it. But, if he has laid his groundwork well, the odds are highly in his favor.

This is where experienced and professional judgment, of course, are of great help but he will use every precaution at his disposal. He will often silk-screen or print up a limited quantity of the package and stack it up in the amounts and under the stacking conditions that he knows exist in that particular area where the product will be found. He will observe it, surrounded by competition. He will pay careful attention to the problem of the package when only the end is seen or when only the sides are seen. He may suggest to the manufacturer that it be tested under actual shelf conditions in certain carefully policed areas, to see if it shows up any weaknesses in actual consumer purchasing. If there is some area of doubt in his mind, he may suggest to the client that he call in a research firm to find certain answers to unknown potential problems.

Now let me pause for a moment to dispel myth number two. A professional package designer is *not* a researcher. He obviously doesn't have the background for it. Some of the methods he uses to find out the facts before he designs may border on research, due to the similarity of techniques, but they are not true research. Certainly a designer is *not* qualified to research the results of his own design. He is, however, well qualified to work with a research organization, to help spell out the problem, and to interpret the results of research back into the

(*Continued on page 126*)

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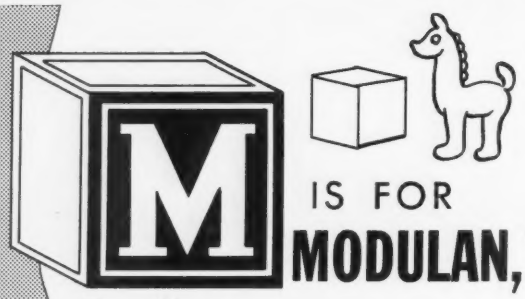

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Yes, MODULAN is above all an emollient. It is lanolin, modified by acetylating the hydroxyl groups to gain extremely valuable new conditioning properties and effects when used on skin and hair.

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MODULAN is hypo-allergenic and non-irritating.

Some of the outstanding characteristics of MODULAN ARE —

Oil soluble, hydrophobic
Substantive yet permeable films
Practically odorless
Soft-waxy, non-tacky protective films
Compatible with o/w emulsions
Compatible with soaps and foams

MODULAN is particularly recommended for use in creams, lotions, baby oils, hair preparations, shaving creams, cream shampoos, lipsticks and ointments.

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AMERCHOL PARK — EDISON, N. J.

(*Continued from page 108*)

plication, and gives promise of far greater usefulness, in medical and pharmaceutical practice.

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BARRIER CREAMS

(*Continued from page 33*)

The cellulose derivatives range from hydrophilic to hydrophobic and vary markedly in degree of protection against various industrial irritants. Methylcellulose and carboxymethylcellulose are most closely related to the natural gums in performance and are hydrophilic.

3. Polymers. In this loose grouping falls one of the most important barrier agents, the high polymers of dimethyl siloxane or silicones. They are quite heat- and cold-stable, oxidation-resistant, odorless and highly water-repellant. Today, there are available new silicone fluids which are compatible with an impressive array of conventional cosmetic ingredients. The silicones rate exceptionally high as barrier agents and have been used successfully in industrial and household moisture-repellant hand preparations, sunscreen lotions, flash-burn protectants and heat-resistant cosmetic bases for television and motion picture use.

SILICONE PROTECTIVE CREAM, GENERAL FORUMLA #1

Silicone oil	40 parts
Magnesium stearate	60 "
	100 "

FLASH-BURN SILICONE PROTECTIVE CREAM, GENERAL FORMULA #2

Silicone oil	50 parts
Titanium dioxide	30 "
Magnesium stearate	18 "
Iron oxide	2 "
	100 "

SILICONE VANISHING HAND CREAM, GENERAL FORMULA #3

Stearic acid	12.0 parts
Silicone fluid	5.0 "
Potassium hydroxide	0.7 "
Triethanolamine	0.3 "
Glyceryl monostearate	2.0 "
Water	80.0 "
Perfume and preservative	q. s.
	100.0 "

Polyvinylpyrrolidone, while usually associated with hair spray preparations, is an excellent film former. Space precludes other than a brief discussion of the more important polymers, but PVP will at least suggest the potentialities of film formers in the development of protective creams.

PVP forms films that are relatively hard. The incorporation of plasticizers will vary the hardness and plasticity of the film. Suitable plasticizing agents comprise diethylene glycol, glycerine, lanolin derivatives, sorbitol and glycerin. PVP is known to reduce the irritating properties of many chemicals and it effectively resists oils. It is insoluble in gasoline, kerosene, turpentine and mineral spirits. Moreover, PVP is compatible with carboxymethylcellulose, gum arabic, cellulose acetate and cetyl alcohol.

Terpene polymers are composed essentially of polymers of pinene. These low-cost products have properties which strongly suggest their suitability in heavy-duty barrier creams. They will effectively resist dilute acids and 10 per cent alkali solutions, but are very soluble in hydrocarbons. Unlike most resins, mineral oil solubility is excellent. Moreover, hydrogenated fats and oleic acid are compatible with this resin.

With the availability of excellent synthetic rubber emulsions, it is predicted that eventually a barrier cream will be formulated so that a peelable rubber film will be deposited on the hands. Apart from the novelty of this product, the protective action of the rubber would of course be high. The silicone rubber compounds might provide even greater protection if a method can be found to incorporate them in a cosmetic base.

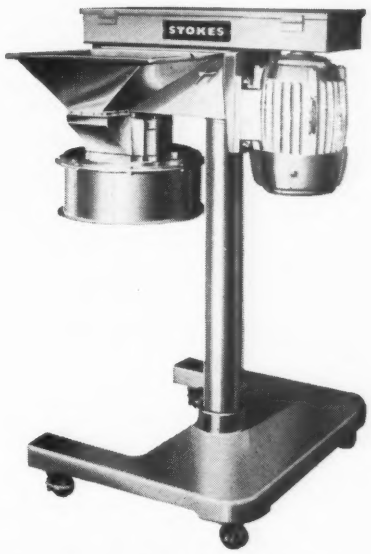
4. Inorganic Compounds. All the products in this grouping are useful film formers. Sodium silicates has been employed in a number of industrial hand preparations, since it resists grease, oils, paints and gasoline and is easily removed.

SILICATE PROTECTIVE CREAM, GENERAL FORMULA #4

Stearic acid	10.0 parts
Glycerine	5.0 "
Potassium hydroxide	0.6 "
Sodium silicate solution	20.0 "
Water	64.4 "
Perfume	q. s.
	100.0 "

Colloidal magnesium aluminum silicate (Veegum) forms very good films in combination with vegetable gums or cellulose derivatives. Heavy metal salts may be used to increase film strength and flexibility. A common plasticizer used in this connection is propylene glycol. Water resistance is said to be improved in products such as polyvinyl alcohol and hydroxyethylcellulose by combinations with colloidal magnesium aluminum silicate.

5 Natural and Hydrocarbon Waxes and Oils. These products are fundamentally hydrophobic with varying emollient action. Some, such as petrolatum, paraffin and ozokerite, produce a waxy or tacky effect, usually followed by a warm, somewhat upleasant sensation on the skin. By themselves, waxes and oils are relatively good protective agents. However, in attempting to improve the cosmetic properties of these materials, some of the protective properties may be



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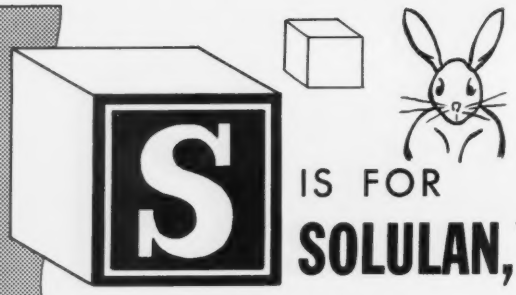

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The SOLULANS are complex — saponification, extraction, purification, esterification, ethoxylation and acetylation are just a few of the steps involved; but these products are worth the effort. Try them and see for yourself.

The SOLULANS are completely soluble in alcohol and in water, and are powerful solubilizers for preparing water solutions of many insoluble substances such as perfumes, antiseptics, dyes, oils and pharmaceuticals.

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Hair preparations	Topical pharmaceuticals
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Shaving creams	Gels and sticks
Colognes	Anti-perspirants
Sunscreens	Deodorants
Insect repellents	Body rubs

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American Cholesterol Products
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AMERCHOL PARK — EDISON, N. J.

altered or lost.

Lanolin is a very good protective agent, as it forms a hydrophobic barrier which clings tightly to the skin. However, there are limits to the quantities employed in a formula, if tackiness is to be avoided. Modified lanolins tend to be less tacky without sacrificing hydrophobic protective properties.

6 Fatty Acids, Esters, Alcohols and Soaps. Stearic acid provides dry, non-greasy films and most hand creams contain this product. The fatty acid esters of low molecular weight alcohols have enjoyed wide popularity in hand creams because they deposit unobjectionable oily and tack-free hydrophobic films on the skin. These esters include butyl stearate, isopropyl stearate, isopropyl palmitate and isopropyl myristate.

Polyol esters, such as glyceryl monostearate and propylene glycol monostearate, develop waxy, water-insoluble films on the hands. The alcohol esters such as cetyl palmitate (spermaceti) are waxy and hydrophilic but cannot be used in high percentages. Fatty alcohols are generally hydrophobic and form non-greasy films. These alcohols would be represented by cetyl and stearyl alcohol.

AEROSOLS

(*Continued from page 45*)

own identifying color, made by Wheaton. The color was carried out even to the actuator, made by Risdon, which also made the important aerosol valve that "engineers" the aerosol dispersal system.

Following the introduction of those five aerosols, the initial order of 300,000 units was an immediate sell-out, and we have been enthusiastic advocates of aerosol packaging ever since.

We now package eight fragrances, having added Voodoo, Danita and Lavender, which is unique in that it is the only Dana fragrance available solely as an aerosol.

Our success in promoting aerosol colognes can be attributed to a variety of factors. First of all, Dana was one of the first major companies in the aerosol field. Secondly, from the start, we packaged our fragrances in attractive and unusual bottles that were clearly identified not only with Dana but also with a specific fragrance. And finally, in an unusual demonstration of faith in aerosols, we "went for broke," putting out five of our six fragrances then on the market in aerosol dispensers.

Curiously enough, teaching retail sales people how to use and sell aerosol colognes was the most difficult part of the introductory period. Since fragrances ultimately must be sold directly to the consumer, much of our success depended on the desire and ability of individual sales people to "sell" one product as against another. Therefore, an informative newsletter was sent to demonstrators, who also received pack-

(*Continued on page 118*)

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Leading Vaginitis and Urethritis Preparations

TRADE NAME	MANUFACTURER	INGREDIENTS	DOSAGE FORM
Gentersal	Ortho	Gentian violet 0.05% Alkyl dimethylbenzyl ammonium chloride 0.05%	Cream
Vag M	KLR Labs	Gentian violet 0.05% Undecylenic acid 0.05% Alum 1.0% Benzoic acid 0.5%	Cream
Gentia Jel	Westwood	Gentian violet 0.1 % Lactic acid 3.0 % Acetic acid (Carbowax base) 1.0 %	Jelly
Gentian Violet Supprettes	Webster	Gentian violet 0.2 % Lactic acid 6.3 % Acetic acid (Water-soluble wax base)	Suppository
Caprylium	Strasenburgh	Sodium caprylate — 3 gms. per pkg. Sodium caprylate *300mg. 10.0 % Zinc caprylate 150mg. 5.0 % Propyl paraamino benzoate 80mg. 4.0 %	Douche Cream *Tablet
Massengill Powder	Massengill	Boric acid, ammonium alum, berberine salt, menthol isamers thymol, eucalyptol, methyl salicylate, phenol	Douche
Merpectogel	Polythress	Phenyl mercuric nitrate (1:24,000) in pectin gel	Jelly
Milibis	Winthrop	Bismuthoxy-p-N-glycolylarsaniiate (in gelatin-glycerine base) 0.25gm.	Suppository
Vagisec	Schmid	Polyoxyethylene nonyl phenol, sodium ethylene dimine tetraacetate, sodium dioctyl sulfosuccinate	Douche, Jelly
Nylmerate	Holland-Rantos	Phenylmercuric acetate 0.02% Boric acid 1.0 % Phenylmercuric acetate in a buffered solvent of alcohol (50.0%), acetone (10.0%) and deionized water 0.2 %	Jelly Douche
Aci-Jel	Ortho	Acetic acid, boric acid, ricinoleic acid, oxyquinoline sulfate, propyl paraban	Jelly
Propion Gel	Wyeth	Calcium propionate 10.0 % Sodium propionate 10.0 % Boric acid 3.0 %	Jelly
Baculin	Amfre	Diiodohydroxyquinoline 100mg. Phenyl mercuric acetate 3mg. Sodium lauryl sulfate 3mg. Lactose 430mg. Dextrose 430.mg Potassium alum 14mg. Papain 20mg.	Tablet Powder
AVC (improved)	National Drug	9-aminoacridine hydrochloride 0.2 % Sulfanilamide 15.0 % Allantoin 2.0 % (with lactose in a water-miscible base buffered with lactic acid to pH 4.5)	Cream
Vacid	Fesler	Polyacrylic resin 1gm.	Tablet
Trichotine	Fesler	Sodium lauryl sulfate, sodium perborate, thymol, sodiumborate, eucalyptol, menthol, methyl salicylate	Douche
Gantrisin	Hoffmann-La Roche	Sulfonamide (3,4-dimethyl-5-sulfanilamido-isoxazole) 10.0 %	Cream
Lorzinex	Maltbie	Sodium lauryl sulfate, benzoic acid, boric acid, p-chlorothymol, lactose, menthol, sodium benzoate, sodium chloride, sodium salicylate, zinc sulfate	Douche
Triva	Boyle	Alkyl aryl sulfonate 35.0 % Ethylene diamine tetra acetic acid 0.3 % Oxyquinoline sulfate 2.0 % Sodium sulfate 53.0 %	Douche
Vioform	Ciba	5-Chloro-7-iodo-8-hydroxyquinoline (41% iodine) 3.0 % " 250gm. " 5gm.	Ointment Cream Tablet Powder
Broxolin	Breon	Bismuth glycobiarsol 0.25gm. " " 5 %	Tablet Cream
Floraquin	Searle	5,7-Diiodo-8-hydroxyquinoline 100mg.	Tablet Powder
Sterisil	Warner-Chilcott	5-amino-1,3-bis-β-ethylhexyl-5-methyl-hexahydro pyrimidine 0.1 %	Jelly
Mycostatin	Squibb	Antibiotic (Squibb Nystatin) 100,000 Units per gm. 500,000 Units	Ointment Oral Tablet
Gyne-plex	Rowell	Tyrothricin, zinc caprylate zinc propionate	Cream

(Continued on page 115)

TRADE NAME	MANUFACTURER	INGREDIENTS		DOSAGE FORM
Gynben	Cambridge	Diiodoquin	100mg.	Tablet
		Sulfadiazine	500mg.	
		Diethylstilbestrol	0.1mg.	
		Sodium lauryl sulfate	6.54mg.	
		Tartaric acid, boric acid, dextrose, lactose, kaolin		
Neosporin Vaginal Suppository	Burroughs-Wellcome	Polymyxin B sulfate	20,500 Units	Tablet
		Neomycin sulfate	5mg.	
		Acetarsone	250mg.	
		Lactose	qs. 1gm.	
Neo-Vagisol	Smith-Dorsey	Tyrothricin	5mg.	Suppository
		Phenyl mercuric acetate	3mg.	
		Succinic acid	12.5mg.	
		Papain	25mg.	
		Sodium lauryl sulfate	3mg.	
Tricofuron	Eaton	Furoxone	0.25%	Suppository
		Furoxone	0.1 %	Powder
Furestrol Urethral	Eaton	Furacin	0.2 %	Suppository
		Diethylstilbestrol	0.0077%	
		Diperodon	2 %	
Furacin Vaginal	Eaton	5-Nitro-2-furaldehyde semicarbazone	0.2 %	Suppository
Furacin Urethral	Eaton	Furacin	0.2 %	Suppository
		Diperodon	2 %	
Triple Sulfa Vaginal	Ortho	Sulfathiazole	3.42%	Cream
		N-Acetyl sulfanilamide	2.86%	
		Benzoylsulfanilamide	3.7 %	
		Urea peroxide	1 %	
Dienestrol Coream	Ortho	Dienestrol	0.1mg./gm.	Cream
Premarin Vaginal	Ayerst	Conjugated estrogens	0.65mg./gm.	Cream

(*Continued from page 31*)

*p*H of the vagina. One Vacid tablet is claimed to maintain the vaginal *p*H at between 4.0 and 4.5 for 24 hours. The recent suggestion that *H. Vaginalis* is a prime causative microbe has given impetus to the sale of Sterisil (Warner-Chilcott).

Numerous drugs have been used for trichomoniasis and moniliasis. The leading chemical agents are phenylmercuric acetate, diiodohydroxyquinoline, bismuth glycobiarsol, caprylates, undecylenates, propionates, aminoacridine and surface active agents. Gentian violet is specific for fungi and is included in numerous preparations, as is the polyene antibiotic

(*Continued on page 116*)

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(Continued from page 115)

nystatin, which is included in the various Squibb dosage forms of Mycostatin. Nystatin is a broad-spectrum fungicide, effective against almost all fungi except actinomyces. It is available as a vaginal suppository, tablets, ointment, dusting powder and as an oral suspension.

Two-fold treatment is quite popular. Since a prime aim is to clean out and dry the vagina, physicians often use a liquid antiseptic to "scrub out." They then prescribe home douche follow-up and the use of another dosage form such as a jelly or suppository as maintenance therapy. Vagisec (Schmid) and Nylmerate (Holland-Rantos) are used in this fashion.

A fourth general type of vaginitis occurs mainly at the "change of life" or menopause. Following the withdrawal of active ovarian function, the vaginal mucosa undergoes atrophic changes that render it thin, pasty and more susceptible to trauma and infection. This condition is frequently termed "senile vaginitis." However, the term is not strictly speaking an accurate one, since the same type of vaginitis may occur in younger women in whom ovarian function has ceased or diminished as a result of various conditions. The vaginal mucosa is subject to inflammation, not only because of the thinness of the mucosa, but also because the mechanism of normal acid production has been impaired, thus permitting the growth of various saprophytes and pathogens. Patients complain chiefly of irritation and tenderness in the genital regions and frequently of an increased irritating vaginal discharge.

The application of estrogen creams, such as Dienestrol Cream (Ortho) or Premarin (Ayerst), affords rapid and specific relief and is extremely valuable in conditioning the vaginal mucosa to be resistant to superimposed infection, often included in such preparations is a mild antiseptic, since there is more susceptibility to infection.

Chronic infections of the female urethra, or urinary canal, are fairly common. By the nature of its structure and position, the urethra is subjected to repeated trauma during childbearing and sexual activity, with the urethral glands serving as admirable lodging places for the retention and growth of microorganisms. The same bacteria noted in vaginitis are found in the urethra, as well as the trichomonas protozoa. Monilia is rarely found.

Therapy consists of instillation of urethral suppositories (bougies) containing antiinfective agents and an anesthetic. Furacin Urethral Suppositories (Eaton) is a prime example, containing the antimicrobial Furacin (2-nitro-2-furaldehyde semicarbazone), and the local anesthetic Diperodon (piperidinopropanediol-diphenylurethane hydrochloride). Senile vaginitis and chronic urethritis often occur together, prompting the belief that there may be a hormonal factor involved in the latter. Bougies containing estrogens, such as Furestrol, (Eaton) are used. END

(*Continued from page 37*)

strated a marked denaturation or dispersion of epidermal horny material.

In studies with aluminum dihydroxy allantoinate, we found it to be an effective mild antiperspirant also demonstrating anti-eczematous properties because of its ability to absorb moisture and its prolonged anti-irritant, healing action. Dusting powders, talcs, creams and lotions containing 0.5 to 1 per cent aluminum dihydroxy allantoinate have been effectively employed in diaper dermatitis because of its acid- and ammonia-consuming properties.

These studies also included clinical observations of the action of a cream containing 0.75 per cent aluminum dihydroxy allantoinate in a glyceryl monostearate base for the treatment of diaper dermatitis and dermatitis venenata due to soap, water, alkalies and detergents. The eczematous eruptions cleared after treatment and the formulation was effectively employed as a prophylactic to prevent the recurrence of these dermatological conditions.

It is our impression that the aluminum dihydroxy allantoinate stimulates healing and forms a coating which acts as a protective agent against contactants. It exerts a prolonged healing and anti-irritant action. No evidence of local irritation or sensitization was noted in the series of 36 patients treated.

In summary, it has now been established that allantoin is non-toxic, non-irritating and non-sensitizing in all concentrations. Further, it has been clinically affirmed that allantoin is a salutary keratolytic, anti-irritant and healing agent.

The introduction of the aluminum allantoinates combining this allantoin action with the bacteriostatic and astringent properties of aluminum now offer new compounds for dermatological research in the treatment of diseases of the pilosebaceous apparatus and the eczematous dermatoses. Personal observations have indicated aluminum chlorhydroxy allantoinate to be particularly effective in antiperspirant-deodorant preparations and for the effective treatment of acne vulgaris. Aluminum dihydroxy allantoinate has proved efficacious in the treatment and prevention of diaper dermatitis and dermatitis venenata. No evidence of primary irritation or sensitization has been observed in the thousands of cases treated with allantoin and aluminum allantoinates.

The aluminum allantoinate preparations used in these clinical studies were supplied by the research departments of Lehn & Fink products Corporation, Reed & Carnrick, and Trudal Laboratories.

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(*Continued on page 118*)

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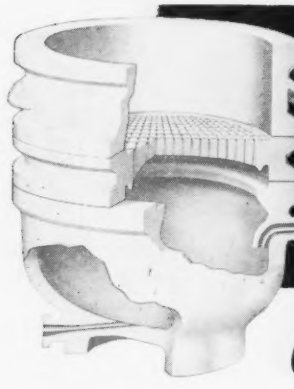

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AEROSOLS

(*Continued from page 112*)

ages of promotional material and other sales aids.

The reception of the aerosols is even more impressive when one realizes that this packaging method has caught on despite the fact that point-of-sale promotion has never been loaded in its favor. We don't use aerosols as counter-testers, it's just too wasteful —every passerby feels compelled to press the actuator, whether or not she's interested in the product. Even so, women still ask for and buy aerosols.

Although aerosols have made an impressive showing in the market place, the customer finally makes her choice primarily on the basis of the fragrance. If she prefers aerosols, she may be influenced to some extent by the color of the package—but this is only a secondary motivating factor. Our best seller in aerosol colognes is packaged in a color that any color psychologist would say is death to sales!

We are now looking into the possibility of equipping our aerosol cologne bottles with metering valves that give off a measured quantity of spray. Although Dana's future plans are a well-guarded secret, one thing is certain—we are in the aerosol fragrance business for keeps.

SKIN RESPIRATION

(*Continued from page 40*)

The respiratory rate was determined in duplicate with readings from left to right and right to left. The results were multiplied with the calibration factor of the vessel and the manometer, in the usual way.

Attention must be paid to some important points when working with the manometric method.

If the amount of tissue used is too large, the rate of oxygen consumption will be determined by the rate at which the oxygen can diffuse from the gas space into the liquid space, and therefore will not represent the respiration rate of the tissue.

The absorption of carbon dioxide by the alkali must be rapid, otherwise considerable errors may occur. The production of carbon dioxide by the respiring tissue should take place at a constant rate. For rapid absorption of carbon dioxide it is advisable to use potassium hydroxide papers.

These tests demonstrate that seawater shows a greater increase in skin respiration than a table salt solution of the same salt content, i.e. 3.4 per cent. If sodium fluoride is added to the sea salt solution, the

oxygen consumption is decreased as compared to the substrate; sodium fluoride acts as an inhibitor. If magnesium sulfate is added, the oxygen consumption is increased; magnesium sulfate thus acts as an activator.

Tests with ointments and cream bases show that cream base No. 3 gives a remarkable increase in skin respiration. Base No. 2 decreases skin respiration, since it contains a greater amount of preservatives, which act as inhibitors. Cream No. 4, a base with an oil containing a high percentage of free fatty acids, shows a large decrease in skin respiration, since fatty acids and some oils act as inhibitors.

The formulas for the ointment and cream bases used in the above tests are given below.

(1) *Polyethylene cream base* (U. S. Patent)
A polyethylene resin of the molecular weight of 21.000 and a m.p. of 110° C. with a heavy mineral gives an excellent gel. This product is stable since, polyethylene is extremely inert, reacting with nothing.

(2) *Ointment base*

Methyl paraben	0.25
Propyl paraben	0.15
Stearyl alcohol	250.00
White petrolatum	250.00
Propylene glycol	120.00
Polyoxylene stearate	50.00
Water	350.00

(3) *Water-washable base*

Glyceryl monostearate	10.0
Propylene glycol	15.0
Cetylmethyl ammonium chloride	0.1
Water	74.9

(4) *Cream with an oil containing a high percentage of free fatty acid.*

In tests with domestic and European varieties of hops, European hops show an oxygen consumption increase as compared with the substrate. Domestic hops show a smaller increase. Since every kind of hops shows a different amount of skin respiration we think that in this way an identification and standardization not only of hops but of other biological materials can be established.

Only one of a number of perfume compounds shows a slight increase in skin respiration as compared with the substrate. One of them shows a slight decrease in skin respiration, and others have no effect. Here, too, we believe, standards can be established and identification made by the manometric method.

Soap has no effect on skin respiration. Anionic and cationic detergents show a small decrease, nonionic detergent shows an increase in skin respiration as compared to the substrate. These tests are not complete since at this writing only one sample of each kind had been tested.

It appears that placenta extract highly stimulates skin respiration, showing very large increases as compared to the substrate. We tested solutions containing 1 per cent, 3 per cent and 5 per cent of placenta extract. A 3 per cent placenta solution shows the greatest increase in skin respiration, at 5 per cent the increase is slightly lower. We therefore believe that the optimum effect is reached with a 3 per cent placenta extract solution. A 1 per cent placenta solution with an added co-enzyme shows almost the same large increase in skin respiration as a 3 per cent solution

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without the co-enzyme.

In conclusion, we believe that the manometric method can become a valuable tool for research and analytical chemistry. The method is simple and with some experience the tests can be made very rapidly. It is possible to standardize every organic preparation and to identify raw materials through manometric methods. With this method it should also be possible to arrive at the optimum effect for skin preparations by measuring their influence on skin respiration and establishing the correct dosages. For the pharmaceutical chemist as well as for the cosmetic chemist, it is of course highly important to know which substances, such as creams, ointment bases, perfume oils, detergents and soaps, are able to stimulate skin respiration. A stimulating effect on the skin is, after all, the purpose of most cosmetics and skin remedies. The method described above enables the chemist to measure the degree of skin respiration. This investigation points out the unusual increase in skin respiration caused by placenta extract. In this way the value and effectiveness of a new product can be determined easily and immediately.

STEROIDS

(*Continued from page 35*)

thrombocythopenic purpura and acute figrinolysis. In leukemia alone, they do the following in greater or lesser degree: (1) act as a "tonic," (2) act as inhibitory or "lytic" agents of lymphoid, splenic, thymic, and plasmocytic tissues; (3) act as possible myelostimulatory agents, thus tending to improve red cell, granulocyte, and platelet production by the bone marrow; (4) act against the auto-antibodies found in the immuno-hemolytic anemia of chronic lymphocytic leukemia and lymphosarcomatosis; (5) modify the course of many cases of acute leukemia in relatively small doses; in massive doses they may often induce complete clinical, hematologic, and bone marrow remissions; (6) possibly reduce the myelotoxic effects of chemotherapeutic agents; (7) improve the bleeding tendency seen in leukemia.

An almost specific effect is induced by adequate dosage of corticosteroids in acute, auto-immune hemolytic anemia. In idiopathic thrombocytopenic purpura, the use of prednisone has revolutionized therapy.

Clinical studies, according to *I. H. Leopold*, revealed the steroid compounds to be effective in a variety of external and internal inflammations, particularly marginal ulcerations of the cornea, anterior uveitis, and allergic external lid and conjunctival inflammations. They have been, with ACTH, of considerable value in the therapy of sympathetic ophthalmia.

Definite contraindications to local as well as systemic steroid therapy have become apparent. Chief

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among these are acute herpes simplex keratitis and fungal keratitis.

For systemic administration, the newer steroids have fewer undesirable side effects but their superior action in cases that have failed to respond to earlier steroids in adequate dosage has not been demonstrated significantly. The advantage of reduced side action may be of great importance for long-term systemic therapy. There are only a few ocular disorders where long-term therapy is justified at present.

In equivalent doses, based on their anti-inflammatory activity, cortisone, hydrocortisone, prednisone, prednisolone, triamcinolone, 6-methyl-prednisolone and dexamethasone all appear to be equally effective in modifying nephrosis, according to *C. M. Riley*. The reduced salt-retaining action of the delta-1 products in the above list makes them preferable in a disease where fluid and salt retention is such a problem.

At present the evidence that steroid treatment in general significantly prolongs life in this condition is excellent.

The anti-inflammatory steroids (AIS) were given by *S. C. Bukantz* to two populations of allergic children. The first comprised 39 ambulant children and the second 150. The latter intractably asthmatic children were admitted from all parts of the U. S. and abroad, and remained in residence for about two years and had usually received AIS, for prolonged periods prior to admission.

The AIS were uniformly effective in controlling allergic symptoms, and by close clinical and laboratory surveillance very few and only minor complications were encountered.

One of the great contributions to dermatology, according to *V. H. Witten*, was the introduction of cortisone and the related corticosteroids. These potent compounds have done much to relieve the suffering associated with many of the diseases of the skin.

The systemic administration of these corticosteroids has made it possible to manage cases of acute self-limited dermatitis, to rehabilitate patients with heretofore disabling dermatoses, and to save the lives of persons with previously fatal diseases of the skin.

These corticosteroids are also effective on external application and they rank among the most valuable topical medicaments ever introduced into dermatologic practice.

A third method of administration, intralesional injection, is also gaining a place.

Comparative dosage schedules for the highly effective dexamethasones for dermatoses in children still must be determined according to *L. Goldman*. From a clinical aspect, topical corticosteroids are more important therapeutic aids in dermatoses in children. Here again, secondary infections in the active child must be prevented even though we are still ignorant of the local mechanism of this reaction.

Local injections of hydrocortisone and the newer analogues still have only a minor therapeutic role in

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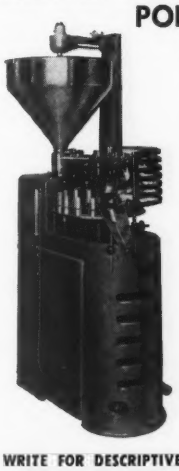

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certain uncommon localized dermatoses in children.

Dexamethasone has been employed by *D. M. Gordon* since May, 1958 in over 70 patients with intra-ocular disease; mainly acute and chronic uveitis. A high degree of success has resulted. Dexamethasone is a highly potent anti-inflammatory steroid and side effects have been minimal. Water retention and acne were the chief and easily managed side effects. Dexamethasone in 0.1 per cent concentration as an eye drop and 0.25 per cent ointment has proved efficacious as a topical application in the same conditions and degree as topical prednisone.

As the new adrenal steroid analogues have appeared, it has become apparent that there may be a great disparity in the relationship between the chemical structure, the anti-inflammatory action and carbohydrate activity of a given steroid. Steroid structure and biological activity, as regards carbohydrate metabolism in man, can often be predicted within only narrow limits.

In other investigations with 21-desoxysteroids, according to *T. F. Frawley*, there is a marked difference between their pituitary corticotrophin suppressing properties and the effect on blood glucose. There arises the problem of ascertaining what effects on carbohydrate metabolism are due to the steroid itself or to the suppression of endogenous adrenal hormone.

FRAGRANT AEROSOLS

(*Continued from page 39*)

sleep in that room must be able to endure the insecticide. Some may remember the days when all insecticides smelled like citronella or wintergreen. Neither odor did a particularly good job of killing the stench of the crude kerosene base, but both did an excellent job of killing the sleep of the party who used the product just before bedtime and of ruining the taste of food when used in the kitchen.

Another important personal product is the hair set. Realizing that the hair is the perfect carrier for fragrance, the manufacturers of hair sets saw to it that this experience should be pleasurable to the customer. Our ladies have a choice between aerosol hair sets from which the fragrance disappears quickly, and those in which the fragrance lingers for a long time. In all instances, however, the odor of the base product is well covered!

There are numerous other items, such as the aerosol shaving creams whose fragrance is never mentioned by the man who uses them but which would not sell unless they were pleasant to his nose, aerosol shampoos, creams and, of course, the most personal of all the aerosols, perfume or toilet water. At this point it might be mentioned that, although fragrance has done much to assure the success of the aerosol, the aerosol in turn should do much to increase the sales of strictly fragrance products, particularly when an attractive purse-sized container is made available on a large scale. Women who have heretofore shied away from carrying purse-size flaconettes of conventional perfume lest spillage ruin the interior of an expensive handbag, have little excuse not to use aerosol perfumes and carry them while shopping or traveling. Incidentally, we in the creative end of the fragrance business are indeed fortunate that the modern tendency of having panels of non-experts decide on what perfumes should be chosen for this or that use has not become as widespread as it once threatened to be. Otherwise, new, intriguing, beautiful and different fragrances would never come into being, for it is an almost universal tendency for lay people to select the existing and the familiar as their first choice when it comes to fragrance.

It is not amazing that innumerable problems faced the perfumer in adapting his fragrances for aerosol use. What is amazing is the relatively short time in which he has solved these problems. We can now satisfy our desire for greater olefactory pleasure, thanks to this gadget, whether we want to deodorize our homes or relieve our aching feet.

What about the future in aerosols? Obviously there is more to come and it is quite likely that the lady of tomorrow will tint her finger nails by means of the aerosol whose flow will be controlled so that just the right amount of polish will cover the nail. Special skin creams to cover freckles and blemishes will also be aerosol-packaged, and it is likely that makeup products will be pressurized. An aerosol leg makeup and an aerosol depilatory will be instrumental in reestablishing the popularity these two items really deserve. The pet owner will benefit and so will the pet when a full line of sprays, germicides and shampoo, wet and dry, for Fido or the cat is available. We must not forget that the aerosol is perfectly suitable for the pharmaceutical field and for edible products. In these areas the aerosol will find a very great potential for expansion.

In connection with the pharmaceutical field, aerosols for inhalation purposes require fragrant "medication," while in the food field the creations of some of the renowned French chefs may be packaged in aerosol to embellish a relatively uninspired meal through the addition of the rich and fragrant odors of the sauces. As for ourselves, we would like to see an aerosol that will dry out a Dry Martini composed of 100 per cent gin, while imparting thereto a delicious flavor.

To turn to matters medical it seems to us that the storage of blood plasma in an aerosol package to be dispensed at a predetermined rate and synchronised with the pulse rate would help the patient, as well as save the time of the trained nurses who must now administer transfusions in the conventional manner.

The American public has been most receptive to so-called "mood music." Why not "mood" fragrances, to create a delicate and unobstrusive atmospheric background that will enhance the decor and the

theme of a room, a festive occasion, or simply create the proper mood for the benefit of one's guests or the family itself. The aeosol, perhaps combined with air conditioning, may well be the answer to this one.

Finally, and at the risk of letting our imaginations run a little wild, it seems to us that aerosols will some day contribute to public health and welfare on a truly grand scale. Sprays capable of sanitizing large areas, for instance, hospitals, subway cars and public buildings, may conceivably so minimize the ravages of airborne bacteria as to all but obliterate the so-called virus infections, as well as the common cold. Should this objective ever be attained we shall have put to use in a practical manner what our ancient forefathers achieved psychologically when they burned incense before the deity for medicinal purposes, so to speak. And, let's not forget that fragrance will continue to play an increasingly important role in the future development of the aerosol.

PATENTS

(*Continued from page 99*)

(5) The Thompson patent is invalid because Thompson was not the original and first inventor of the subject matter thereof.

(6) Claims 1 and 2 of the Thompson patent, which include the use of gelatin in ACTH without added ingredients, are not entitled to the filing date of Thompson's parent application in August, 1950, because the parent application did not teach the use of ACTH in gelatin without added ingredients.

(7) The Thompson patent is invalid because Armour publicly sold ACTH-gelatin compositions in the fall of 1951, more than a year prior to the filing date of Thompson's continuation-in-part application filed in December, 1952.

(8) The Thompson patent is invalid because Thompson's original application claimed that Thompson was the inventor of ACTH and PVP, which was the suggestion of Dr. Wolfson.

(9) The Thompson patent was secured after furnishing the Patent Office with false and misleading evidence and statements, and this invalidates the Thompson patent.

(10) Commercial success will not serve to validate an otherwise invalid patent.

Findings of Fact—Bunding Patent

(1) Plaintiff owns the Bunding Patent in suit, No. 2,669,536, which was issued on February 16, 1954 on an application filed August 15, 1950.

(2) The Bunding patent describes a method of purifying ACTH by adsorbing the ACTH on an adsorbent and then eluting the ACTH therefrom in more purified form.

(3) The three claims of the Bunding patent call for adsorption on "cellulose material," the pH of ad-

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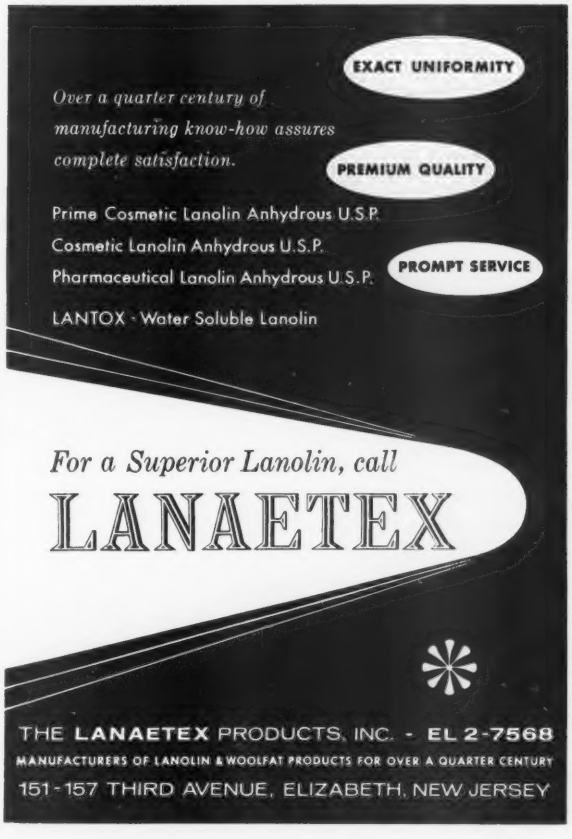
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sorption being above 3, and the pH of elution being below the pH of adsorption and within the range of 1.0 to 4.5.

(4) The essential features of the Bunding patent are (a) the use of a "natural cellulose" adsorbent and (b) the use of a mild acid solution for adsorption and a strong acid solution for elution.

(5) The only "natural cellulose" adsorbents referred to in the Bunding patent are Solka Floc and filter paper.

(6) Defendant is charged with infringement of all three claims of the Bunding patent, but only for a period from March 30, 1954, to September 23, 1954, when defendant used an adsorption pH above 3.0.

I. *Defendant does not infringe the Bunding patent.*

(7) In June, 1951, Dr. E. B. Astwood of Boston published a paper in the Journal of the American Chemical Society, describing a process for the purification of ACTH employing oxycellulose as an adsorbent.

(8) Defendant adopted the Astwood process for purification of ACTH and has always used oxycellulose as an adsorbent.

(9) Defendant obtains approximately the same yield of purified ACTH per pound of pituitary glands (18,000-27,000 subcutaneous units; 6,000-9,000 intravenous units) employing oxycellulose powder at a pH sometimes below 3 and sometimes above 3 as plaintiff obtains at a pH of 4 (8,000 intravenous units) using oxycellulose gauze.

(10) The Bunding patent does not mention oxycellulose or suggest its use; Bunding never used oxycellulose.

(11) Armour was unaware of work done with oxycellulose before Dr. Astwood's publication. Immediately after publication of Dr. Astwood's article, Dr. Fisher of Armour was notified of the article, Dr. Hays of Armour went to see Dr. Astwood, and Armour adopted the Astwood process.

(12) The Bunding patent application as originally filed claims "an adsorbent" or "paper." Promptly after publication of the Astwood article, Bunding amended his claims to substitute the term "cellulose material" for the terms "an adsorbent" and "paper."

(13) In his arguments attempting to distinguish over the prior art, Bunding alleged, in addition to arguments with respect to pH, that there was patentability in the "specific adsorbents" and "limited group of adsorbents" employed by Bunding, which were, of course, only Solka Floc and filter paper.

(14) The Bunding patent is not infringed by defendant unless the term "cellulose material" appearing in each of the claims includes oxycellulose.

(15) Plaintiff agrees that the use of exycellulose was the invention of Dr. Astwood and that the use of oxycellulose is the Astwood method, irrespective of the pH employed. Plaintiff acknewlodged that Dr. Astwood is one of the most capable medical scientists in America today; Dr. Astwood did not apply for a patent on his invention of the use of oxycellulose, thereby making it freely available to the world.

(16) Oxycellulose is not "natural cellulose," which is an essential feature of the Bunding patent; oxycellulose is cellulose which has been oxidized by nitrogen dioxide.

(17) Oxycellulose is a different chemical substance than natural cellulose. Oxycellulose contains acid carboxyl groups and dissolves in sodium hydroxide, whereas cellulose is not acid and will not dissolve in sodium hydroxide.

(18) The Bunding patent calls for 50 grams (50,000 milligrams) of cellulose to purify one gram of ACTH, whereas only 0.08 grams (80 milligrams) of oxycellulose are used to purify the same amount of ACTH, that is, 625 times as much cellulose as oxycellulose is required to purify an equivalent amount of ACTH.

(19) The tiny amount of oxycellulose used to purify 1 gram of ACTH (80 milligrams) gives far greater purification than the large amount of Solka Floc (50,000 milligrams).

(20) If oxycellulose is substituted for cellulose and used in accordance with the process set forth in the Bunding patent, no purification is obtained.

(21) If the term "celulose materials" includes materials other than "natural cellulose" referred to in the Bunding patent, it equally includes materials such as wood flour, cellophane and many other materials that include the term "cellulose" as a part of their names, such as cellulose acetate butyrate, all of which will not work.

(22) Claims of the Bunding patent call for elution from the adsorbent at a pH between 1.0 and 4.5; when ACTH is adsorbed on oxycelulose, it cannot be eluted from the oxycellulose at a pH of 4.0, showing that oxycellulose is not equivalent to cellulose.

(23) Oxycellulose is not "cellulose material."

(24) The Bunding patent is not infringed by defendant's purification process employing oxycellulose.

II. *Bunding was not the first inventor.*

(25) About the middle of August, 1949, Bunding noted that ACTH could be adsorbed on cellulose at a pH of 2.5. On August 31, 1949, Bunding did some work on paper strip chromatograms, but could not tell which component was ACTH and which component was an impurity. Paper strip chromatography was a well-known and commonly used technique in 1949. As of August 31, 1949, Bunding had no conception of the invention claimed in his patent.

(26) Bunding's next work appears in an undated paper strip chromatographic experiment (the samples were assayed on December 30, 1949) wherein Bunding learned that ACTH could be adsorbed on cellulose and separated from its impurities, but no mention is made as to the adsorption pH. On January 4, 1950, in another paper strip chromatographic

experiment, Bunding postulated conditions for separating ACTH from its impurities and recovering it in purified form by adsorption on paper and subsequent elution therefrom. Bunding had not as yet achieved increased purity or satisfied himself that all the necessary conditions for his process had been determined, and he conducted additional experiments in January, 1950 at adsorption pH's between 6 and 9 using filter paper as an adsorbent.

(27) On January 25, 1950, Bunding realized that he could achieve an increase in purity and he outlined a method which formed the basis for his patent.

(28) In March, 1950, Bunding prepared an invention disclosure which claims January 25, 1950 as the conception date of his invention.

(29) As of January 25, 1950, the only cellulose material used by Bunding was filter paper; the record does not show that Bunding ever worked with Solka Floc or any other natural cellulose.

(30) The invention claimed by Bunding in his patent was not conceived by Bunding until January 25, 1950.

(31) Bunding's testimony with respect to his dates of invention was uncorroborated and, hence, there is a failure of proof of any date of invention prior to his filing date of August 15, 1950.

(32) There is a serious danger of overdosage with ACTH, and the only way to test the utility of purified ACTH is clinically, in human beings.

(33) Bunding never clinically tested cellulose purified ACTH; and no other Armour witness was able to say whether cellulose purified ACTH was ever clinically tested by Armour. ACTH purified by adsorption on cellulose has never been used commercially.

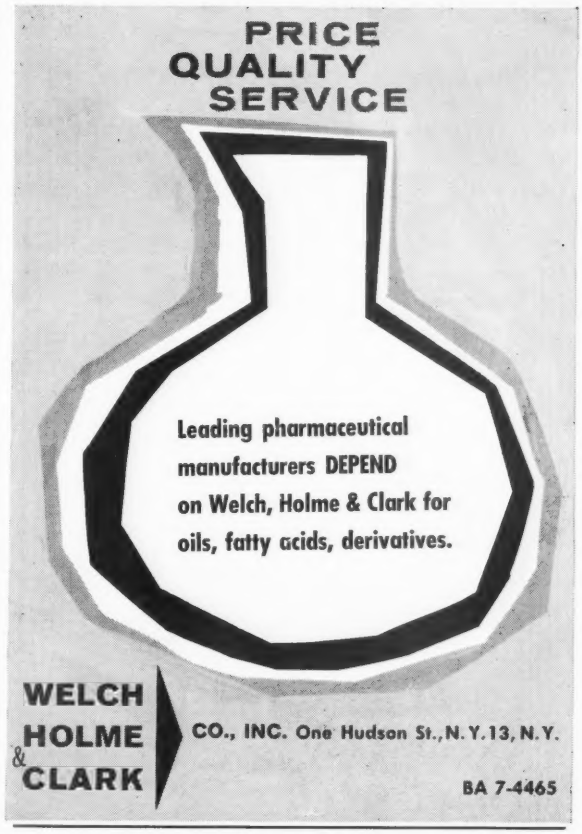
(34) Bunding did not reduce to practice his invention relating to the purification of ACTH with cellulose until it was constructively reduced to practice by the filing of his application for patent on August 15, 1950 because he failed properly to test the product.

(35) Dr. E. B. Astwood of Boston purified ACTH by adsorbing it on cellulose (Solka Floc) on December 10, 1949, and eluting the ACTH therefrom with hydrochloric acid. On January 14, 15, and 19, 1950, Dr. Astwood adsorbed ACTH on Solka Floc (cellulose) in 1/10 normal acetic acid and eluted purified ACTH therefrom with 1/10 normal hydrochloric acid. This is the process of the Bunding patent.

(36) Dr. Astwood clinically tested ACTH purified by cellulose in February, 1950. This was a reduction to practice of the invention. The results of Dr. Astwood's work and clinical testing of cellulose purified ACTH were reported in a paper published in September, 1950.

(37) Dr. Astwood's testimony was fully corroborated by his associate, Dr. Raben.

(38) Dr. Astwood conceived the process claimed in the Bunding patent before Bunding, and Dr. Astwood reduced the process to practice before Bunding.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(39) Dr. Astwood was the first inventor of the process described and claimed in the Bunding patent.

Conclusions of Law-Bunding Patent

(1) The Bunding patent is not infringed by Defendant's method of purification of ACTH, which employs oxycellulose.

(2) If the Bunding patent is interpreted to include other materials than natural cellulose, then the Bunding patent includes inoperative substances and is invalid. Hence it is not infringed by the Astwood oxycellulose process.

(3) Bunding is not entitled to the invention dates claimed by him, because Bunding's testimony was uncorroborated.

(4) It was necessary for Bunding to show utility of his invention to reduce it to practice.

(5) In order to establish utility of the method claimed in the Bunding patent and hence reduction to practice, the purified ACTH produced by the method required clinical testing.

(6) In the absence of an actual reduction to practice, the filing of a patent application constitutes a constructive reduction to practice.

(7) Bunding's invention was not completed until it was constructively reduced to practice by the filing of his patent application in August, 1950; an invention is only completed by reduction to practice—mere conception is not sufficient.

(8) The Bunding patent is invalid because Astwood, and not Bunding, was the first inventor of the subject matter claimed in the Bunding patent.

(9) The Bunding patent is unenforceable against defendant because plaintiff did not come with clean hands in respect of any cause of action in this case in view of the mispropriety of the prosecution of the Thompson patent in the Patent Office.

RECENT PATENTS

2,857,375-6—Schenley—Streptomycin and Dihydrostreptomycin Salts.

2,857,383—G. D. Searle—Amino Esters of Thianaphthenealkanoic Acids.

2,857,384—Ciba—Pyridazones.

2,857,385—Ciba—Pentacyclic Lactones.

2,857,386—Ciba—Iso Reserpic and Iso Deserpidic Acids.

2,857,388—Ciba—3-Epiallo-Yohimlenes.

2,857,390—Sterling Drug—Mono-Quaternary Ammonium Salts of Bis-Tertiary-Aminoalkyl Amides of Alkanedioic Acids.

2,857,391—Merck—Aminomethylbenzimidazoles.

PACKAGE DESIGNER

(*Continued from page 109*)

realm of package design.

After the design has been approved, what next? The package designer must see it through its final art form into the printed product. He must be totally

responsible for the basic production of the new design until it is ready to leave for the market. He must be thoroughly conversant with materials, printing methods and printing results. He must give careful attention to the container that will carry the product in quantities to the market. He must know the rules of proper identification of these containers. He must know how they are handled in warehouses and distribution points and the information that the handlers must know quickly.

After the product is finally out on the shelf, what next? In most cases, nothing, except to watch it move from the shelf. In rare cases where trouble develops, he must know how to find out the facts and how to make the correction. Is he always 100 per cent right? Of course not. Is the doctor always right? Does the doctor always give you the right prescription the first time? But his batting average is tremendously higher than yours would be if you tried to treat your own disease.

This brings us to myth number three, which concerns the amount of bragging that has been done by some of us in the profession, in which staggering statistics have been offered as to how much good the new package has done for a product. True, there are isolated cases where packaging alone has done a tremendous job, but the best package in the world will sell a poor product only once.

Packaging is only one phase of today's complicated selling and merchandising operation. Of course it is an important phase. After the product has been made, after it has been advertised properly, after it has been distributed to the retailer, and after it has been put on the shelf, then it must stand alone and become the final link in a powerful chain. But no package, no matter how well-designed, can perform miracles. Don't expect it to. Don't use packages as a crutch—consider a well-designed package to be as important a piece of equipment as is a well-designed piece of machinery for handling and sealing that same package.

The services of a package designer should be used at every phase of an operation. They should be considered when the manufacturer is first thinking about a new product. The package designer's problems should be taken into account and he should be consulted when you are starting to manufacture the product. He should have an opportunity to consider the problem of the jobber and the distributor, as well as that of the retailer.

By bringing a package designer in at the very beginning, you will get the most for your money. Very often a package designer is only called upon as a last resort when the packaging situation is very sick. At that point, the manufacturer runs panic-stricken to a professional designer and expects overnight miracles. There are as yet no wonder drugs for packaging problems, and there are as yet no wonder workers in the package design profession.

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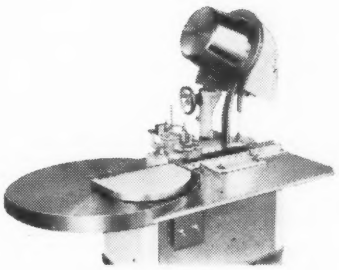

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American Cholesterol Products, Inc. 106, 108, 110, 112
American Sterilizer Co. 80
Anchor Hocking Glass Co. 60-61
Armour Pharmaceutical Co. 116

Baker Chemical Co., J. T. 10

Calumet Manufacturing Co. 46
Camilli, Albert & Laloue, Inc. 130
Carr-Lowrey Glass Co. 56
Cavalla, Inc., A. 126
Charabot & Co., Inc. 7
Colonial Applicator Co. 58B
Colton Co., Arthur 117
Columbia-Southern Chemical Corp. 5
Continental Can Co. 42
Continental Oil Co. 4
Croda, Inc. 15
Crown Cork & Seal Co., Inc. 50B

Delta Chemical Works 129
Distillation Products Industries 20
Dodge & Olcott, Inc. 9
Dow Corning Corp. 18
Dragoco, Inc. 66A
Durlin Co. 8B

Eastman Chemical Products, Inc. 96
Emery Industries, Inc. 105
Encapsulations, Inc. 121
Ertel Engineering Corp. 116

Fairmount Chemical Co., Inc. 126
Firmenich Incorporated 8A
Florasynth Labs., Inc. 12
Fritzsche Brothers, Inc. ....90A, B and C

Gane's Chemical Works 119
Givaudan-Delawanna, Inc. ....24A and B, 103
Glycerine Producers Association 6
Griffin-Rutgers, Inc. 129
Groen Manufacturing Co. 77

Harchem Div., Wallace & Tiernan, Inc. 115
Haring Equipment Corp. 121
Heyden-Newport Chemical Corp. 24A
Hoffmann-La Roche Aromatics Div. ....16A and B
Hoffmann-La Roche, Inc. 1, 70
Huisking & Co., Inc., Charles L. 13

Ising Corp., C. E. 129
Ivers Lee Co. 57

Kohnstamm & Co., H. 66B
Kolar Labs., Inc. 8

Lambert Engraving Co. 48
Lanaetex Products, Inc., The 123
Lautier Fils 92
Lueders & Co., George 16

Mallinckrodt Chemical Works 24D
Maryland Glass Corp. 52
Mathieu, Inc., Charles 126
Metalsmiths Div. of Orange Roller Bearing Co. 119
Metro Glass Co., Inc. 50A

Newman-Green, Inc. 75
New Jersey Zinc Co., The 109
New York Quinine & Chemical Works 22
Norda Essential Oil & Chemical Co. ....Cover 2

Parson Plymouth, Inc., M. W. 120
Peerless Tube Co. 58A
Penick & Co., S. B. 68
Pennsylvania Refining Co. 113
Pfaltz & Bauer, Inc. 129
Pfizer & Co., Inc., Chas. ....Cover 4
Popper & Sons, Inc. 127
Precision Valve Corp. 76
Progressive Machine Works 129

Reheis Co., Inc. 84
Richford Corp. 54
Ritter & Co., F. 127
Robinson Wagner Co., Inc. 64

Scientific Associates 129
Scranton Aerosol Packaging 129
Standard Pharmacal Co. 125
Sterwin Chemicals, Inc. 3
Stokes Corp., F. J. 82-83, 111
Synfleur Scientific Labs., Inc. 101

Ungerer & Co. ....Cover 3
Union Carbide Chemicals Co. 44, 95
U. S. Bottlers Machinery Co. 100
U. S. Industrial Chemicals Co., Div. of Nat'l Distillers & Chemical Corp. 98A and B
U. S. Stoneware 118

van Ameringen-Haebler, Inc 62, 88-89
Vanderbilt Co., R. T. 72
Van Dyk & Co., Inc. 97
Verley & Co., Albert 11
Verona Chemical Co. 14
Vitamerican Oil Corp. 118

Wallerstein Co. 87
Welch, Holme & Clark Co. 125
Western Condensing Company 91
Will & Baumer Candle Co., Inc. 107
Wallace & Tiernan, Inc. 115